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Clinical paper

# Functional outcomes among survivors of pediatric in-hospital cardiac arrest are associated with baseline neurologic and functional status, but not with diastolic blood pressure during CPR

***Heather A. Wolfe[a,*], Robert M. Sutton[a], Ron W. Reeder[b], Kathleen L. Meert[c], Murray M. Pollack[d,k], Andrew R. Yates[e], John T. Berger[d], Christopher J. Newth[f], Joseph A. Carcillo[g], Patrick S. McQuillen[h], Rick E. Harrison[i], Frank W. Moler[j], Todd C. Carpenter[l], Daniel A Notterman[m], Richard Holubkov[b], J. Michael Dean[b], Vinay M. Nadkarni[a], Robert A. Berg[a], for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) Pediatric Intensive Care Quality of Cardiopulmonary Resuscitation (PICqCPR) Investigators[1]***

[a] *Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA United States*
[b] *Department of Pediatrics, University of Utah, Salt Lake City, UT United States*
[c] *Department of Pediatrics, Children's Hospital of Michigan, Wayne State University, Detroit, MI United States*
[d] *Department of Pediatrics, Children's National Medical Center, Washington, D.C. United States*
[e] *Department of Pediatrics, Nationwide Children's Hospital, The Ohio State University, Columbus, OH United States*
[f] *Department of Anesthesiology, Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, CA United States*
[g] *Department of Critical Care Medicine, Children's Hospital of Pittsburgh, University of Pittsburgh, Pittsburgh, PA United States*
[h] *Department of Pediatrics, Benioff Children's Hospital, University of California San Francisco, San Francisco, CA United States*
[i] *Department of Pediatrics, Mattel Children's Hospital, University of California Los Angeles, Los Angeles, CA United States*
[j] *Department of Pediatrics, C.S. Mott Children's Hospital, University of Michigan, MI United States*
[k] *Department of Pediatrics, Phoenix Children's Hospital, Phoenix, AZ United States*
[l] *Department of Pediatrics, Denver Children's Hospital, University of Colorado, Denver, CO United States*
[m] *Department of Molecular Biology, Princeton University, Princeton, NJ United States*

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*Abbreviations:* CPR, Cardiopulmonary resuscitation; CPCCRN, Collaborative Pediatric Critical Care Research Network; PICqCPR study, Pediatric Intensive Care Quality of CPR study; DBP, Diastolic blood pressure; SBP, Systolic blood pressure; ROSC, Return of spontaneous circulation; ICU, intensive care unit; CoPP, coronary perfusion pressure; PCPC, Pediatric cerebral performance category; FSS, Functional Status Scale; DCC, Data Coordinating Center.

* Corresponding author at: The Children's Hospital of Philadelphia, The University of Pennsylvania Perelman School of Medicine, 3401 Civic Center Blvd, Wood Building Rom 6040, Philadelphia, PA 19104-4399, United States.

E-mail address: wolfeh@email.chop.edu (H.A. Wolfe).

[1] A complete list of the CPCCRN PICqCPR Investigators appears in Appendix A.

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## Abstract

**Aim:** Diastolic blood pressure (DBP) during cardiopulmonary resuscitation (CPR) is associated with survival following pediatric in-hospital cardiac arrest. The relationship between intra-arrest haemodynamics and neurological status among survivors of pediatric cardiac arrest is unknown.

**Methods:** This study represents analysis of data from the prospective multicenter Pediatric Intensive Care Quality of cardiopulmonary resuscitation (PICqCPR) Study. Primary predictor variables were median DBP and median systolic blood pressure (SBP) over the first 10 min of CPR. The primary outcome measure was "new substantive morbidity" determined by Functional Status Scale (FSS) and defined as an increase in the FSS of at least 3 points or increase of 2 in a single FSS domain. Univariable analyses were completed to investigate the relationship between new substantive morbidity and BPs during CPR.

**Results:** 244 index CPR events occurred during the study period, 77 (32%) CPR events met all inclusion criteria as well as having both DBP and FSS data available. Among 77 survivors, 32 (42%) had new substantive morbidity as measured by the FSS score. No significant differences were identified in DBP (median 30.5 mmHg vs. 30.9 mmHg, $p = 0.5$) or SBP (median 76.3 mmHg vs. 63.0 mmHg, $p = 0.2$) between patients with and without new substantive morbidity. Children who developed new substantive morbidity were more likely to have lower pre-arrest FSS than those that did not (median [IQR]: 7.5 [6.0–9.0] versus 9.0 [7.0–13.0], $p = 0.01$).

**Conclusion:** New substantive morbidity determined by FSS after a pediatric IHCA was associated with baseline functional status, but not DBP during CPR.

**Keywords:** Cardiopulmonary resuscitation (CPR), Cardiac arrest, Pediatric, In-hospital, Survival, Outcomes

## Introduction

In-hospital cardiac arrest (IHCA) affects >200,000 patients in the United States annually, with approximately 5–10,000 children per year requiring cardiopulmonary resuscitation (CPR) during their hospital stay.[1,2] At least partly due to the success of increased implementation of early warning systems and rapid response teams, almost all pediatric IHCA occurs in a pediatric intensive care unit (PICU).[3] While CPR training has traditionally stressed mechanics of CPR (e.g., absolute measurement-based compression depth or rate), many of these ICU patients will have invasive haemodynamic monitoring in place at the time of the arrest that could be used to guide the resuscitation effort.[3] To that end, the 2015 Pediatric Advanced Life Support (PALS) Guidelines suggested that the use of physiology to guide resuscitation was reasonable; however, there was insufficient evidence at the time to recommend actual blood pressure targets to guide pediatric CPR and no evidence on how this may affect short or long-term outcomes.[4]

In a recent large cohort study published by this group, diastolic blood pressure (DBP) ≥25 mmHg during CPR in infants and ≥30 mmHg in children ≥1 year old was associated with greater likelihood of survival to hospital discharge and survival with favorable neurologic outcome.[5] This study was an important first step in defining optimal blood pressure targets during CPR in children. In this study 91% of the children who survived had a favorable neurologic outcome defined using the Pediatric Cerebral Performance Category (PCPC) Score, a standard neurological assessment recommended by the Utstein Guidelines for uniform reporting of cardiac arrest studies.[6] Despite 'good' PCPC scores, 30% of survivors had new substantive morbidity when measured with the more granular Functional Status Scale (FSS). New substantive morbidity is defined as an increase in the FSS by at least 3 points or an increase of at least 2 in a single FSS domain and indicates a significant worsening in functional status. Although previous studies have demonstrated that the PCPC and the FSS correlate well, the FSS does not rely on subjective assessments by clinicians or research assistants and may be more sensitive to subtle changes in neurological status.[7,8] The high rate of new substantive morbidity suggests that PCPC may have underestimated neurological injury in this study cohort and it is not known if the DBP threshold attained in this study is different in patients with or without new substantive morbidity.

Thus, we evaluated whether or not the same BP targets that were associated with survival to hospital discharge are associated with less functional morbidity among survivors from the Pediatric Intensive Care Quality of CPR (PICqCPR) Study of the Collaborative Pediatric Critical Care Research Network (CPCCRN). Our primary hypothesis was that mean DBP ≥ 25 mmHg during CPR in infants and ≥30 mmHg in children ≥1 year old would be associated with a lower risk of new substantive morbidity among survivors. Our secondary hypotheses were: (1) mean compression phase ("systolic") blood pressure (SBP) ≥60 mmHg in infants and ≥80 mmHg in children ≥1 year old would also be associated with a lower risk of new substantive morbidity among survivors; and (2) that both mean DBP and SBP during CPR would be higher among patients without new substantive morbidity.

## Methods

The CPCCRN PICqCPR Study was a prospective multicenter cohort study of ICU CPR conducted across 11 institutions. During this study, Pediatric ICU (PICU) or Pediatric Cardiac ICU (CICU) patients who received chest compressions for ≥1 min and had invasive arterial blood pressure monitoring during CPR were enrolled between July 1, 2013 and June 30, 2016. To be included in the parent study, patients were required to have invasive arterial BP monitoring during CPR as well as central venous pressure, respiratory plethysmography or ECG artifact to allow determination of CPR starts and stops. Participating sites identified cardiac arrests via a paging system and/or daily research coordinator screening procedures. The project was approved with waiver of informed consent by the Institutional Review Board at each clinical site and the University of Utah Data Coordinating Center (DCC).

CPCCRN research coordinators obtained Utstein-style standardized cardiac arrest and CPR data,[6] including demographics, preexisting conditions, illness categories, interventions in place at time of arrest, first documented rhythm, immediate cause of arrest, duration of CPR, resuscitation interventions, and outcome data, with assessments of neurological outcomes by Pediatric Cerebral Performance Categories (PCPC) and functional status by Functional Status Scale (FSS)[8] scores for pre-admission status and at hospital discharge. The FSS contains 6 domains of function, including mental status, sensory functioning, communication, motor functioning, feeding and respiratory status. Each domain is categorized from normal (score = 1) to very severe dysfunction (score = 5) and the range of possible scores are 6–30.

De-identified arterial waveforms were manually digitized and analyzed by Children's Hospital of Philadelphia investigators (PlotDigitizer; Version 2.0; Department of Physics, University of South Alabama) who were blinded to clinical data and survival outcome. During this process, numerical X (time in seconds) and Y (arterial BP) data were extracted. Mean DBP and mean SBP were determined for each minute of CPR, and mean DBP and mean SBP for each patient was the average BP over the first 10 min of CPR. For patients with $<$10 min of CPR, the mean BPs could only be determined for the minutes of CPR provided. Please see previous publication for more details regarding parent study methods and arterial blood pressure determination.[5]

Statistical Analysis

The overall goal of this secondary analysis was to evaluate the association of DBP with functional status among survivors, and to identify other factors that may be related to functional outcome among survivors of pediatric IHCA. The primary outcome of this secondary analysis is new substantive morbidity defined as an increase in the FSS total score of at least 3 or an increase of at least 2 in a single FSS domain.

Patient and event characteristics were summarized using median and quartiles or frequencies and percentages. Differences in these characteristics between patients with and without new substantive morbidity were examined using Fisher's exact test for categorical variables or the Wilcoxon rank-sum test for ordinal variables. P-values are reported based on a 2-sided alternative and considered statistically significant when $\le$0.05. All analyses were performed using SAS software v9.4 (Cary, NC).[9–15]

## Results

There were 244 index CPR events that occurred during the study period, of which 77 (32%) CPR events met all inclusion criteria as well as having both DBP as well as FSS data available. Fig. 1 is a consort-style diagram of included and excluded patients. Table 1 describes pre-arrest characteristics in the entire cohort of included patients, as well as comparisons of these characteristics between children who survived with and without new substantive morbidity. The majority of the cohort had normal or mild disability based on baseline PCPC scores; 32 normal PCPC (42%) and 26 mild disability (34%) respectively. Of patients with the pre-existing condition of pneumonia, none developed new substantive morbidity (new substantive morbidity 0 (0%) vs no new substantive morbidity 8 (18%); p = 0.018). The baseline median FSS score for the overall cohort was 8, with a significantly lower baseline FSS for patients who developed new substantive morbidity compared with those who did not (median [IQR]: baseline FSS 7.5 [6.0, 9.0] vs 9.0 [7.0, 13.0], p = 0.01).

Event characteristics for the overall cohort as well as those with and without new substantive morbidity are displayed in Table 2. Immediate cause of arrest included hypotension in 49 (64%), respiratory decompensation in 34 (44%), and arrhythmia in 14 (18%). These survivors had median DBP of 31 mmHg, median SBP of 69 mmHg, median chest compression rate of 113 and median chest compression fraction of 0.9. Median duration of CPR was 5 min. There

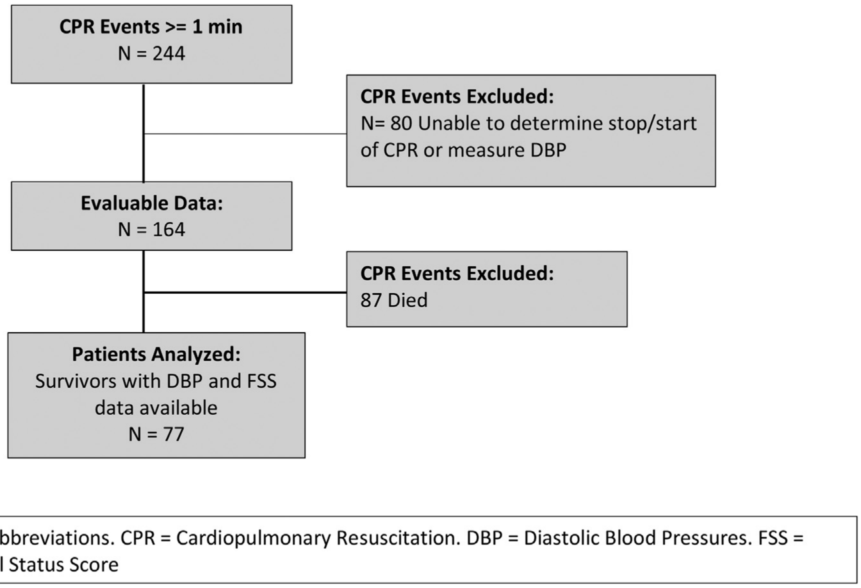

**Fig. 1 – Utstein-style flow diagram of patients included in analysis.**
**Abbreviations: CPR = cardiopulmonary resuscitation. DBP = Diastolic Blood Pressures. FSS = Functional Status Score**
**Legend: Abbreviations. CPR = cardiopulmonary resuscitation. DBP = Diastolic Blood Pressures. FSS = Functional Status Score**

**Table 1 – Pre-arrest characteristics by new substantive morbidity.**

| | New substantive morbidity | | | |
|---|---|---|---|---|
| | Overall(N = 77) | Yes(N = 32) | No(N = 45) | P-value |
| Age | | | | 0.07[a] |
| <1 month | 22 (29%) | 6 (19%) | 16 (36%) | |
| 1 month – <1 year | 31 (40%) | 12 (38%) | 19 (42%) | |
| 1 year – <8 years | 14 (18%) | 10 (31%) | 4 (9%) | |
| 8 years – <19 years | 10 (13%) | 4 (13%) | 6 (13%) | |
| Male | 47 (61%) | 18 (56%) | 29 (64%) | 0.49[a] |
| Race | | | | 0.06[a] |
| White | 37 (48%) | 20 (63%) | 17 (38%) | |
| Black or African American | 12 (16%) | 4 (13%) | 8 (18%) | |
| Other | 5 (6%) | 0 (0%) | 5 (11%) | |
| Not reported | 23 (30%) | 8 (25%) | 15 (33%) | |
| Preexisting conditions | | | | |
| Respiratory insufficiency | 59 (77%) | 23 (72%) | 36 (80%) | 0.43[a] |
| Hypotension | 51 (66%) | 22 (69%) | 29 (64%) | 0.81[a] |
| Congestive heart failure | 7 (9%) | 5 (16%) | 2 (4%) | 0.12[a] |
| Pneumonia | 8 (10%) | 0 (0%) | 8 (18%) | 0.02[a] |
| Sepsis | 20 (26%) | 6 (19%) | 14 (31%) | 0.30[a] |
| Renal insufficiency | 8 (10%) | 5 (16%) | 3 (7%) | 0.27[a] |
| Malignancy | 1 (1%) | 0 (0%) | 1 (2%) | 1.00[a] |
| Congenital heart disease | 55 (71%) | 24 (75%) | 31 (69%) | 0.62[a] |
| Illness category | | | | 0.50[a] |
| Surgical cardiac | 49 (64%) | 20 (63%) | 29 (64%) | |
| Medical cardiac | 8 (10%) | 5 (16%) | 3 (7%) | |
| Surgical non-cardiac | 5 (6%) | 2 (6%) | 3 (7%) | |
| Medical non-cardiac | 14 (18%) | 4 (13%) | 10 (22%) | |
| Unknown | 1 (1%) | 1 (3%) | 0 (0%) | |
| Baseline pediatric cerebral performance category | | | | 0.43[b] |
| Normal | 32 (42%) | 13 (41%) | 19 (42%) | |
| Mild disability | 26 (34%) | 15 (47%) | 11 (24%) | |
| Moderate disability | 13 (17%) | 2 (6%) | 11 (24%) | |
| Severe disability | 6 (8%) | 2 (6%) | 4 (9%) | |
| Baseline functional status scale | 8.0 [6.0, 11.0] | 7.5 [6.0, 9.0] | 9.0 [7.0, 13.0] | 0.01[b] |

[a] Fisher's exact test is used for categorical variables.

[b] The Wilcoxon rank-sum test is used for ordinal variables.

was no significant difference in CPR quality (chest compression rate, chest compression fraction and both DBP and SBP achieved during CPR) among those who survived with or without new substantive morbidity. First documented rhythm was most frequently bradycardia with poor perfusion in 52 (68%) events, followed by 20 (26%) events with asystole/PEA. Interventions in place at the time of arrest were vasoactive infusions in 53 (69%) patients and invasive mechanical ventilation in 57 (74%) patients. Sixty-five (84%) patients received epinephrine during their resuscitation. There was no significant difference in event characteristics among those who survived with or without new substantive morbidity. There was a trend towards new substantive morbidity in patients who received sodium bicarbonate during their resuscitation (59% with vs 38% without new substantive morbidity, p = 0.07).

Table 3 includes the summary of outcomes among this cohort. Sixty-four (83%) achieved ROSC and 13 (17%) achieved return of circulation with the aid of extracorporeal membrane oxygenation (ECMO). Survival with favorable neurologic outcome was achieved in 70 (91%) of patients based on PCPC scores (normal, mild and moderate PCPC scores). PCPC scores were normal in 24 (31%), mild disability in 27 (35%), moderate disability in 17 (22%), severe disability in 8 (10%) and coma/vegetative state in 1 (1%). Functional Status Scale scores in survivors were classified as good in 12 (16%), mildly abnormal in 27 (35%), moderate disability in 31 (40%), severely abnormal in 4 (5%) and very severely abnormal in 3 (4%). Fig. 2 shows the overlap in distribution of scores between FSS and PCPC.

New substantive morbidity at hospital discharge was present in 32 (42%) of survivors. Patients who were normal or only had mild disability by PCPC or FSS scores at baseline were more likely to have worse functional status at hospital discharge than those with neither PCPC $\leq 2$ or FSS $\leq 9$ based on an increase in FSS $> 2$ in one category (Table 4). For patients with normal or mild disability there was a trend toward developing new substantive morbidity at hospital discharge based on an increase in overall FSS score of $>3$.

**Table 2 – Event characteristics by new substantive morbidity.**

| | New substantive morbidity | | | |
|---|---|---|---|---|
| | Overall(N = 77) | Yes(N = 32) | No(N = 45) | P-value |
| Avg. Haemodynamics over (up to) the first 10 min | | | | |
| DBP (mmHg) | 30.9 [25.0, 38.7] | 30.5 [23.5, 37.0] | 30.9 [25.0, 38.7] | 0.53[a] |
| SBP (mmHg) | 69.0 [53.8, 93.0] | 76.3 [58.5, 97.4] | 63.0 [51.8, 89.0] | 0.20[a] |
| Compression rate (/minute) | 113.4 [92.8, 129.2] | 107.8 [89.9, 120.4] | 117.7 [95.4, 130.0] | 0.13[a] |
| Chest compression fraction | 0.9 [0.8, 1.0] | 0.9 [0.8, 1.0] | 0.9 [0.8, 1.0] | 0.73[a] |
| Mean DBP above target[d] | 55 (71%) | 20 (63%) | 35 (78%) | 0.20[b] |
| Mean SBP above target[e] | 44 (57%) | 21 (66%) | 23 (51%) | 0.25[b] |
| Avg. Haemodynamics 6–10 min prior to the arrest (N = 66) | | | | |
| Mean Arterial Pressure (mmHg) | 54.3 [46.0, 69.6] | 51.6 [46.0, 65.0] | 58.2 [46.0, 69.6] | 0.69[a] |
| DBP (mmHg) | 43.0 [36.0, 52.0] | 43.0 [35.6, 49.6] | 43.7 [36.4, 53.1] | 0.66[a] |
| SBP (mmHg) | 77.8 [57.6, 94.0] | 68.2 [55.6, 90.8] | 80.5 [59.2, 97.7] | 0.52[a] |
| Location of CPR Event | | | | 0.46[b] |
| PICU | 23 (30%) | 8 (25%) | 15 (33%) | |
| CICU | 54 (70%) | 24 (75%) | 30 (67%) | |
| Immediate cause | | | | |
| Hypotension | 49 (64%) | 23 (72%) | 26 (58%) | 0.24[b] |
| Respiratory decompensation | 34 (44%) | 11 (34%) | 23 (51%) | 0.17[b] |
| Arrhythmia | 14 (18%) | 8 (25%) | 6 (13%) | 0.24[b] |
| First documented rhythm at time CPR initiated (Collapsed) | | | | 1.00[b] |
| Asystole/PEA | 20 (26%) | 8 (25%) | 12 (27%) | |
| VF/VT | 5 (6%) | 2 (6%) | 3 (7%) | |
| Bradycardia with poor perfusion | 52 (68%) | 22 (69%) | 30 (67%) | |
| Duration or CPR (minutes) | 5.0 [2.0, 13.0] | 5.0 [2.5, 12.0] | 5.0 [2.0, 14.0] | 0.88[a] |
| Duration of CPR (minutes) | | | | 0.95[c] |
| 1–5 | 43 (56%) | 18 (56%) | 25 (56%) | |
| 6–10 | 19 (25%) | 8 (25%) | 11 (24%) | |
| 11–35 | 8 (10%) | 3 (9%) | 5 (11%) | |
| >35 | 7 (9%) | 3 (9%) | 4 (9%) | |
| Interventions in place | | | | |
| Central venous catheter | 66 (86%) | 27 (84%) | 39 (87%) | 1.00[b] |
| Vasoactive infusion | 53 (69%) | 21 (66%) | 32 (71%) | 0.63[b] |
| Invasive mechanical ventilation | 57 (74%) | 21 (66%) | 36 (80%) | 0.19[b] |
| Non-invasive ventilation | 11 (14%) | 6 (19%) | 5 (11%) | 0.51[b] |
| Time[g] | | | | 0.70[b] |
| Weekday | 51 (66%) | 20 (63%) | 31 (69%) | |
| Weeknight | 11 (14%) | 6 (19%) | 5 (11%) | |
| Weekend | 15 (19%) | 6 (19%) | 9 (20%) | |
| Pharmacologic interventions | | | | |
| Epinephrine | 65 (84%) | 28 (88%) | 37 (82%) | 0.75[b] |
| # of doses (when used) | 2 [1,3] | 2 [1,4] | 2 [1,3] | 0.23[a,f] |
| Calcium | 28 (36%) | 15 (47%) | 13 (29%) | 0.15[b] |
| Sodium bicarbonate | 36 (47%) | 19 (59%) | 17 (38%) | 0.07[b] |

[a] The Wilcoxon rank-sum test is used for continuous variables.

[b] Fisher's exact test is used for categorical variables.

[c] The Cochran–Armitage test for trend is used for duration of CPR category variables.

[d] Target DBP is ≥25 for infants and ≥30 for children.

[e] Target SBP is ≥60 for infants and ≥80 for children.

[f] The comparison of # of epinephrine doses is based only on index events for which epinephrine was used.

[g] Weekdays are Mon–Fri, 07:00–22:59; weeknights are Mon–Fri, 23:00–06:59; and weekends are Sat–Sun.

## Discussion

In this multicenter study of pediatric in-hospital cardiac arrest, haemodynamics during CPR were not associated with functional outcomes among survivors at the time of discharge. Specifically, children who attained mean DBP ≥ 25 mmHg during CPR in infants and ≥30 mmHg in children ≥1 year old did not have a lower risk of new substantive morbidity among survivors. In addition, there were no differences in either mean DBP or SBP among subjects with and without new substantive morbidity. These findings were consistent among infants <1 year and children >1 year. Children with new substantive morbidities had significantly better baseline FSS scores compared to children who did not develop new substantive morbidity post-arrest. Children who were normal or only mild disabled by PCPC and FSS scales at pre-arrest baseline were more likely to have worse functional status at hospital discharge. Differences in short term functional outcomes may be related to other unmeasured pre-arrest, intra-arrest, or post-arrest factors.

**Table 3 – Summary of outcomes.**

| | Overall(N = 77) |
|---|---|
| Immediate outcome | |
| ROSC[a] $\geq$ 20 min | 64 (83.1%) |
| ROC with E-CPR[b] | 13 (16.9%) |
| Hospital discharge outcomes | |
| Survival with favorable neurologic outcome[c,d] | 70 (90.9%) |
| Pediatric Cerebral Performance Category | |
| Normal | 24 (31.2%) |
| Mild disability | 27 (35.1%) |
| Moderate disability | 17 (22.1%) |
| Severe disability | 8 (10.4%) |
| Coma/vegetative state | 1 (1.3%) |
| Functional Status Score (FSS) in survivors | |
| Good (6–7) | 12 (15.6%) |
| Mildly abnormal (8–9) | 27 (35.1%) |
| Moderately abnormal (10–15) | 31 (40.3%) |
| Severely abnormal (16–21) | 4 (5.2%) |
| Very severely abnormal (22–30) | 3 (3.9%) |
| FSS change from baseline in survivors | 0.0 [0.0, 3.0] |
| New Substantive Morbidity at Hospital Discharge[e] | 32 (41.6%) |

[a] ROSC, Return of Spontaneous Circulation.

[b] E-CPR, Extracorporeal cardiopulmonary resuscitation.

[c] Survival was assumed for 1 subject alive who remained in the hospital 6 months after CPR at the end of the study. FSS and PCPC were obtained at that time for this assumed survivor.

[d] Favorable neurologic outcome defined as discharge PCPC of normal, mild disability, or moderate disability or a discharge PCPC no worse than baseline PCPC.

[e] New substantive morbidity is defined as an increase of at least 3 between baseline and discharge FSS or an increase of 2 or more in a single domain.

Previous studies of pediatric IHCA have shown that improvements in chest compression quality are associated with higher odds of survival to discharge with favorable neurologic outcomes.[16,17] The definition of favorable neurologic outcome in the majority of studies is a PCPC score of 1–3 or unchanged from baseline. This definition is consistent with the Utstein-style recommendations for neurologic assessment after cardiac arrest and is the scoring system utilized in cardiac arrest registries such as the American Heart Association Get With the Guidelines-Resuscitation registry. The parent PICqCPR study established a relationship between survival to hospital discharge with favorable neurologic status (using PCPC score) with adjusted relative risk of 1.6 when mean DBP during the early minutes of CPR was maintained at thresholds of ≥25 mmHg in infants and ≥30 mmHg in children ≥1 year old compared to those who did not attain this threshold DBP. Survivors in the parent study had excellent neurologic outcomes with 91% having good neurologic outcome based on PCPC scoring; however, approximately 30% of survivors had a new substantive functional morbidity based on FSS score (substantial new morbidity defined as increase in the FSS score of at least 3).[5]

We were unable to demonstrate an association between FSS scores and DBP achieved during CPR despite the relationship between DBP and survival with favorable neurologic outcomes seen in the parent study. The functional status scale was developed to measure adaptive behavior, similar to activities of daily living. The PCPC score is a subjective *cerebral* scale that relies on the impression of observers or data abstractors and ranges from normal, mild, moderate, severe disability and vegetative state/coma (1–5).[18] As such, the PCPC score lacks precision and in large studies, it was necessary to group PCPC categories to attain good interrater reliability. In prior studies the FSS and PCPC correlated well within the normal and mild categories; however, there was significant

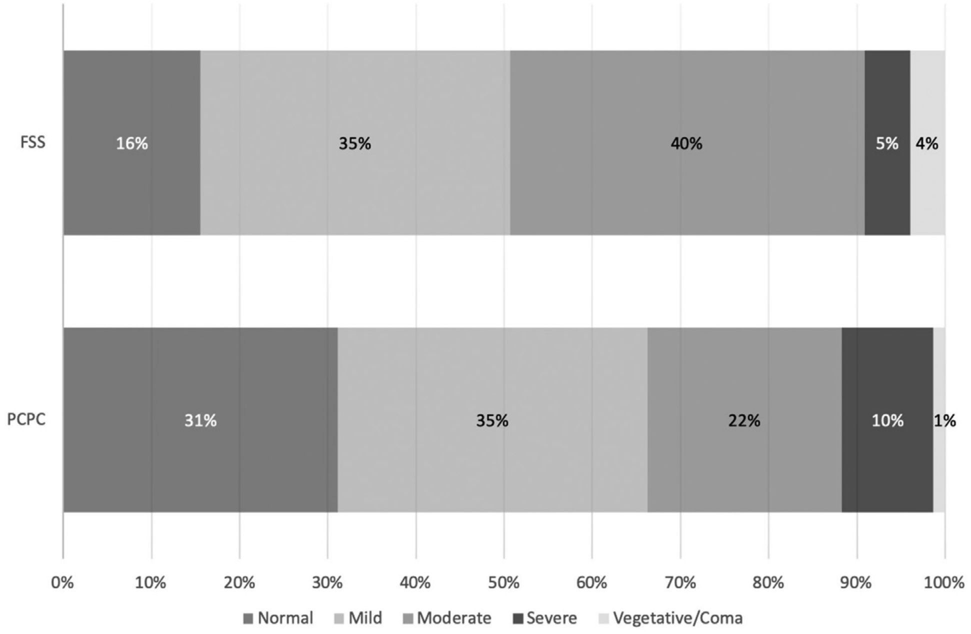

**Fig. 2 – Distribution of FSS scores vs. PCPC scores.**

**FSS and PCPC scores among survivors at discharge. FSS = Functional Status Scale. PCPC = Pediatric Cerebral Performance.**

**Table 4 – Outcomes by baseline status.**

| | Normal or mild disability at baseline[a] | | |
|---|---|---|---|
| | Yes (N = 62) | No (N = 15) | P-value |
| New morbidity at hospital discharge (Change in FSS> = 3 from baseline) | 21 (33.9%) | 1 (6.7%) | 0.05[b] |
| Increase of 2  or more in a single FSS domain | 28 (45.2%) | 2 (13.3%) | 0.04[b] |

[a] FSS ≤ 9 or PCPC ≤ 2.
[b] Fisher's exact test.

dispersion in the FSS scores within moderate and severe PCPC categories.[7] In addition, for a patient to be considered ‘favorable outcome’ with the PCPC scale they could have had a change from normal to moderate disability; however, a fair portion of these patients were not included as good outcome based on an FSS change of 3. The two scales measure separate but overlapping attributes, as the FSS is measuring *functional* status versus the PCPC measuring *cerebral* status (e.g., the neurologic assessment including communication, mental status and sensory functioning overlap with the PCPC score, but FSS score includes other attributes such as respiratory function). The FSS is less reliant on subjective measures than the PCPC score and may be a superior way to define *functional* outcome in future studies of pediatric resuscitation.

These data suggest that normal and near-normal infants and children are at especially high risk for new morbidity and changes in functional status post-arrest. This finding may be related to two distinct or overlapping explanations. It is possible that discerning a substantial change is easier in normal or near normal children than it is in children with significant functional disabilities. For example, a normal child that develops swallowing dysfunction and mild language difficulty after cardiac arrest that required a gastrostomy tube for feeding would have an increase in FSS score of 4 points and move from the normal to moderately abnormal category. The need for a new gastrostomy tube in a child who does not walk and has limited vocabulary at baseline would not have a change in the FSS score. Alternatively, children with normal or only mild functional disability may have higher baseline oxygen consumption, and therefore may be more vulnerable to injury from the hypoxic-ischemic insult of cardiac arrest. Future studies investigating neurologic and functional outcomes post-arrest should consider controlling for pre-arrest baseline status.

Neurologic and functional outcomes after cardiac arrest is multifactorial in nature and quality of CPR during arrest is only one factor influencing the functional outcome. Baseline neurologic status, medical history, specific patient characteristics, duration of no-flow or low-flow time, and post-cardiac arrest care all also play a role in the eventual neurologic and functional outcome of the patient. For example, post-arrest fever[19] and hypotension in the first 6 h after arrest are associated with worse hospital discharge neurologic outcomes.[20] Conversely, normocarbia after cardiac arrest is associated with improved neurologic outcomes compared to hypercarbia (defined as $pCO2 > 50$ mmHg).[21] In the present study we were not able to control for many potentially important pre-arrest characteristics, intra-arrest factors or post-arrest care variables. Larger studies with more detailed pre-arrest, intra-arrest and post-cardiac arrest data collection will need to be performed to fully delineate the relative importance of these elements of care on neurologic and functional outcome.

While this study did not show an association between blood pressure during CPR and functional neurologic outcomes, adequate BP during CPR is important. The main study clearly associated higher DBP with improved survival outcomes. After this threshold is reached and ROSC is obtained, meticulous attention to post-arrest care may be the driving force behind improving neurologic outcomes in cardiac arrest. Similarly, the mean SBP was not associated with improved functional outcomes among survivors of in-hospital cardiac arrest. While not statistically significant, patients with new substantive morbidity tended to have *higher* average systolic blood pressures during CPR. Finally, children with new substantive morbidity had lower baseline FSS than those without.

It is important that we address limitations of this current study. Because only 32 patients survived with a new substantive morbidity, the study may have been underpowered to demonstrate an association of BP during CPR with functional status; however, the median DBP during CPR was nearly identical in the two groups (30.5 versus 30.9 mmHg). The intra-arrest haemodynamic data was only recorded for the first 10 min of CPR for each case due to practical limitations of data collection. This precluded our ability to detect the relationship of blood pressures and neurologic outcomes beyond the first 10 min of CPR; however, the median duration of CPR was 5.0 min [interquartile range: 2.0, 13.0 min] and only one-third of the patients had much longer than 10 min of CPR. The participating sites are all large academic pediatric ICUs which may have more resource availability and ability to provide care during and after cardiopulmonary arrest than other sites. The quality of CPR provided to patients in this study was better than previously published studies on cardiac arrest and these findings may not apply across all settings. There are many associations with new morbidity including age, severity of illness, chronic health status that are also related to cardiac arrest status and assessment of this complex relationship is limited in a study of this sample size. Finally, functional status scale at the time of discharge represents a relatively short term neurologic outcome and longer term measures may show different results.

## Conclusions

Worse functional status after a pediatric in-hospital cardiac arrest was associated with baseline neurologic and functional status, but not blood pressure during CPR.

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## Conflicts of interest

The Authors have the following disclosures. Dr. Wolfe has received research funding from NHLBI (funds to institution), as well as speaking honoraria from Zoll Medical. Robert A Berg received research grants from NHLBI and NICHD to study pediatric in-hospital cardiopulmonary resuscitation (funds to institution), as well as speaking honoraria from Japan Pediatric Society for lecture on pediatric cardiopulmonary resuscitation. Dr. Sutton has received research grants from NHLBI and NICHD to study pediatric in-hospital cardiopulmonary resuscitation (funds to institution), Pediatric Advance Life Support authorship via the American Heart Association, membership on the Emergency Cardiovascular Care Committee and past speaking honoraria for Zoll Medical. The rest of the authors report no COI.

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## Appendix A.

**Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) Pediatric Intensive Care Quality of Cardiopulmonary Resuscitation (PICqCPR) Investigators:** Athena F. Zuppa, Katherine Graham, Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA United States; Carolann Twelves, Mary Ann Diliberto, Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA United States; Elyse Tomanio, Department of Pediatrics, Children's National Medical Center, Washington, D.C. United States; Jeni Kwok, Department of Anesthesiology, Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, CA United States; Michael J. Bell, Department of Pediatrics, Children's National Medical Center, Washington, D.C. United States; Department of Critical Care Medicine, Children's Hospital of Pittsburgh, University of Pittsburgh, Pittsburgh, PA United States; Alan Abraham, Department of Critical Care Medicine, Children's Hospital of Pittsburgh, University of Pittsburgh, Pittsburgh, PA United States; Anil Sapru, Department of Anesthesiology, Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, CA United States; Department of Pediatrics, Benioff Children's Hospital, University of California San Francisco, San Francisco, CA United States; Mustafa F. Alkhouli, Department of Pediatrics, Benioff Children's Hospital, University of California San Francisco, San Francisco, CA United States; Sabrina Heidemann, Ann Pawluszka, Department of Pediatrics, Children's Hospital of Michigan, Wayne State University, Detroit, MI United States; Mark W. Hall, Lisa Steele, Department of Pediatrics, Nationwide Children's Hospital, The Ohio State University, Columbus, OH United States; Thomas P. Shanley, Department of Pediatrics, C.S. Mott Children's Hospital, University of Michigan, MI United States; Department of Pediatrics, Lurie Children's Hospital, Northwestern University, Chicago, IL United States; Monica Weber, Department of Pediatrics, C.S. Mott Children's Hospital, University of Michigan, MI United States; Heidi J. Dalton, Department of Pediatrics, Phoenix Children's Hospital, Phoenix, AZ United States; Aimee La Bell, Peter M. Mourani, Department of Pediatrics, Denver Children's Hospital, University of Colorado, Denver, CO United States; Kathryn Malone, Department of Pediatrics, Denver Children's Hospital, University of Colorado, Denver, CO United States; Russell Telford, Christopher Locandro, Whitney Coleman, Alecia Peterson, Julie Thelen, Department of Pediatrics, University of Utah, Salt Lake City, UT United States; Allan Doctor, Department of Pediatrics, Washington University School of Medicine, St. Louis, MO United States.

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