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**Corresponding Author:** Kathleen Meert, MD, Department of Pediatrics, Children's hospital of Michigan, Central Michigan University, 3901 Beaubien, Detroit, Mi 48201, USA; Phone 1-313-745-5870; kmeert@dmc.org.

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Credit Author Statement

| Author | Role |
|---|---|
| Katherine Cashen | Conceptualization, Methodology, Writing - Original Draft, Writing - Review & Editing |
| Robert M Sutton | Conceptualization, Methodology, Investigation, Resources, Data Curation, Writing - Review & Editing, Supervision, Funding acquisition |
| Ron W Reeder | Methodology, Software, Validation, Formal analysis, Resources, Data Curation, Writing - Review & Editing |
| Tageldin Ahmed | Investigation, Resources, Writing - Review & Editing |
| Michael J Bell | Investigation, Resources, Writing - Review & Editing |
| Robert A Berg | Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| Candice Burns | Investigation, Resources, Writing - Review & Editing |
| Joseph A Carcillo | Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| Todd C Carpenter | Investigation, Resources, Writing - Review & Editing |
| J Michael Dean | Resources, Data Curation, Writing - Review & Editing, Supervision, Funding acquisition |
| J Wesley Diddle | Investigation, Resources, Writing - Review & Editing |
| Myke Federman | Investigation, Resources, Writing - Review & Editing |
| Ericka L Fink | Investigation, Resources, Writing - Review & Editing |
| Deborah Franzon | Investigation, Resources, Writing - Review & Editing |
| Aisha H Frazier | Investigation, Resources, Writing - Review & Editing |
| Stuart H Friess | Investigation, Resources, Writing - Review & Editing |
| Kathryn Graham | Investigation, Resources, Writing - Review & Editing |
| Mark Hall | Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| David A Hehir | Investigation, Resources, Writing - Review & Editing |
| Christopher M Horvat | Investigation, Resources, Writing - Review & Editing |
| Leanna L Huard | Investigation, Resources, Writing - Review & Editing |
| Theresa Kirkpatrick | Investigation, Resources, Writing - Review & Editing |
| Tensing Maa | Investigation, Resources, Writing - Review & Editing |
| Arushi Manga | Investigation, Resources, Writing - Review & Editing |
| Patrick S McQuillen | Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| Ryan W Morgan | Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| Peter M Mourani | Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| Vinay M Nadkarni | Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing |
| Maryam Y Naim | Investigation, Resources, Writing - Review & Editing |
| Daniel Notterman | Writing - Review & Editing, Supervision |
| Kent Page | Software, Validation, Formal analysis, Data Curation, Writing - Review & Editing |

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# Calcium Use during Paediatric In-hospital Cardiac Arrest is Associated with Worse Outcomes

**Katherine Cashen, DO**[1], **Robert M Sutton, MD, MSCE**[2], **Ron W Reeder, PhD**[3], **Tageldin Ahmed, MD**[4], **Michael J Bell, MD**[5], **Robert A Berg, MD**[2], **Candice Burns, MD**[6], **Joseph A Carcillo, MD**[7], **Todd C Carpenter, MD**[8], **J Michael Dean, MD**[3], **J Wesley Diddle, MD**[5], **Myke Federman, MD**[9], **Ericka L Fink, MD, MS**[7], **Deborah Franzon, MD**[10], **Aisha H Frazier, MD, MPH**[11,12], **Stuart H Friess, MD**[13], **Kathryn Graham, MLAS**[2], **Mark Hall, MD**[14], **David A Hehir, MD**[2], **Christopher M Horvat, MD**[7], **Leanna L Huard, MD**[9], **Theresa Kirkpatrick, MSN, CNS**[9], **Tensing Maa, MD**[14], **Arushi Manga, MD**[13], **Patrick S McQuillen, MD**[10], **Ryan W Morgan, MD, MTR**[2], **Peter M Mourani, MD**[15], **Vinay M Nadkarni, MD, MS**[2], **Maryam Y Naim, MD, MSCE**[2], **Daniel Notterman, MD**[16], **Kent Page, MStat**[3], **Murray M Pollack, MD**[5], **Danna Qunibi, MD**[14], **Anil Sapru, MD**[9], **Carleen Schneiter, MD**[8], **Matthew P Sharron, MD**[5], **Neeraj Srivastava, MD**[9], **Shirley Viteri, MD**[11,12], **David Wessel, MD**[5], **Heather A Wolfe, MD, MSHP**[2], **Andrew R Yates, MD**[14], **Athena F Zuppa, MD**[2], **Kathleen L Meert, MD**[4]

[1]Department of Pediatrics, Duke Children's Hospital, Duke University, 2301 Erwin Road, Durham, NC, 27710, USA;

[2]Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, University of Pennsylvania, 34th Street and Civic Center Blvd, Philadelphia, PA, 19104, USA;

[3]Department of Pediatrics, University of Utah, 295 Chipeta Way, P.O. Box 581289, Salt Lake City, UT, 84158, USA;

[4]Department of Pediatrics, Children's Hospital of Michigan, Central Michigan University, 3901 Beaubien Blvd, Detroit, MI, 48201, USA;

| Author | Role |
|---|---|
| Murray M Pollack | Investigation, Resources, Writing - Review & Editing, Funding acquisition |
| Danna Qunibi | Investigation, Resources, Writing - Review & Editing |
| Anil Sapru | Investigation, Resources, Writing - Review & Editing |
| Carleen Schneiter | Investigation, Resources, Writing - Review & Editing |
| Matthew P Sharron | Investigation, Resources, Writing - Review & Editing |
| Neeraj Srivastava | Investigation, Resources, Writing - Review & Editing |
| Shirley Viteri | Investigation, Resources, Writing - Review & Editing |
| David Wessel | Investigation, Resources, Writing - Review & Editing |
| Heather A Wolfe | Investigation, Resources, Writing - Review & Editing |
| Andrew R Yates | Conceptualization, Methodology, Investigation, Resources, Writing - Review & Editing |
| Athena F Zuppa | Investigation, Resources, Writing - Review & Editing |
| Kathleen L Meert | Conceptualization, Methodology, Investigation, Resources, Writing - Original Draft, Writing - Review & Editing, Supervision, Funding acquisition |

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[5]Department of Pediatrics, Children's National Hospital, George Washington University School of Medicine, 111 Michigan Ave, NW, Washington, DC,20010, USA;

[6]Department of Pediatrics and Human Development, Michigan State University, 100 Michigan St, NE, Grand Rapids, MI, 49503, USA;

[7]Department of Critical Care Medicine, UPMC Children's Hospital of Pittsburgh, University of Pittsburgh, One Children's Hospital Drive, 4401 Penn Ave, Pittsburgh, PA, 15224, USA;

[8]Department of Pediatrics, Children's Hospital Colorado, University of Colorado School of Medicine, 13121 East 17th Ave, Aurora, CO, 80045, USA;

[9]Department of Pediatrics, Mattel Children's Hospital, University of California Los Angeles, 757 Westwood Plaza, Los Angeles, CA, 90095, USA;

[10]Department of Pediatrics, Benioff Children's Hospital, University of California-San Francisco, 1845 Fourth Street, San Francisco, CA, 94158, USA;

[11]Nemours Children's Hospital, Delaware, 1600 Rockland Rd, Wilmington, DE, 19803, USA;

[12]Department of Pediatrics, Sidney Kimmel Medical College, Thomas Jefferson University, 1025 Walnut Street, Philadelphia, PA, 19107, USA;

[13]Department of Pediatrics, St. Louis Children's Hospital, Washington University School of Medicine, One Children's Place, St. Louis, MO, 63110, USA;

[14]Department of Pediatrics, Nationwide Children's Hospital, The Ohio State University, 700 Children's Drive, Columbus, OH, 43205, USA;

[15]Department of Pediatrics, University of Arkansas for Medical Sciences and Arkansas Children's Research Institute, 13 Children's Way, Little Rock, AR, 72202, USA;

[16]Department of Molecular Biology, Princeton University, 119 Lewis Thomas Laboratory, Washington Road, Princeton, NJ, 08544, USA; and the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN) and National Heart Lung and Blood Institute ICU-RESUScitation Project Investigators

## Abstract

**Aim:** To evaluate associations between calcium administration and outcomes among children with in-hospital cardiac arrest and among specific subgroups in which calcium use is hypothesized to provide clinical benefit.

**Methods:** This is a secondary analysis of observational data collected prospectively as part of the ICU-RESUScitation project. Children 37 weeks post-conceptual age to 18 years who received chest compressions in one of 18 intensive care units from October 2016-March 2021 were eligible. Data included child and event characteristics, pre-arrest laboratory values, pre-and intra-arrest haemodynamics, and outcomes. Outcomes included sustained return of spontaneous circulation (ROSC), survival to hospital discharge, and survival to hospital discharge with favourable neurologic outcome. A propensity score weighted cohort was used to evaluate associations between calcium use and outcomes. Subgroups included neonates, and children

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with hyperkalaemia, sepsis, renal insufficiency, cardiac surgery with cardiopulmonary bypass, and calcium-avid cardiac diagnoses.

**Results:** Of 1,100 in-hospital cardiac arrests, median age was 0.63 years (IQR 0.19, 3.81); 450 (41%) received calcium. Among the weighted cohort, calcium use was not associated with sustained ROSC (aOR, 0.87; CI95 0.61–1.24; p=0.445), but was associated with lower rates of both survival to hospital discharge (aOR, 0.68; CI95 0.52–0.89; p=0.005) and survival with favourable neurologic outcome at hospital discharge (aOR, 0.75; CI95 0.57–0.98; p=0.038). Among subgroups, calcium use was associated with lower rates of survival to hospital discharge in children with sepsis and renal insufficiency.

**Conclusions:** Calcium use was common during paediatric in-hospital cardiac arrest and associated with worse outcomes at hospital discharge.

### Keywords

cardiopulmonary resuscitation; cardiac arrest; calcium; neonate; infant; child

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## INTRODUCTION

Over 15,000 paediatric in-hospital cardiac arrests (IHCA) occur in the United States annually.[1,2] The American Heart Association (AHA) guidelines recommend that routine calcium administration during paediatric cardiopulmonary resuscitation (CPR) should be avoided and the use of calcium should be limited to specific circumstances during cardiac arrest which include documented hypocalcaemia, hyperkalaemia, hypomagnesaemia, and calcium channel blocker overdose.[3,4] Calcium administration during paediatric CPR remains common; however, multiple studies have reported no benefit from calcium use and some studies have reported harm.[5–9]

Previous studies of calcium use during paediatric IHCA have been single-centre or registry reports. A multicentre study utilizing data from the National Registry of Cardiopulmonary Resuscitation (NRCPR) characterized calcium use during paediatric IHCA.[9] The study reported calcium was used frequently during CPR in paediatric facilities and its use was associated with cardiac surgery, intensive care unit (ICU) settings, duration of CPR >15 minutes, asystole and concurrent use of other advanced life support medications. Calcium use was associated with decreased rates of survival to hospital discharge and survival with favourable neurologic outcome at hospital discharge. Although that study contributed significantly to our knowledge of calcium use during paediatric IHCA, it was limited by its observational nature and the data elements included in the registry. In the current study, we aim to characterize the use of calcium in a propensity score weighted cohort of children undergoing CPR in paediatric ICUs with detailed prospective child, event and haemodynamic data.

The primary objective of our study was to assess the relationships between calcium use during paediatric IHCA and outcomes. Outcomes included sustained return of spontaneous circulation (ROSC) >20 minutes, survival to hospital discharge, survival to hospital discharge with favourable neurologic outcome, and functional status at hospital discharge.

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We also report child and event characteristics, and pre- and intra-arrest haemodynamics associated with calcium use. Finally, we evaluated calcium use among pre-specified subgroups that included neonates (≤ 1 month), children with hyperkalaemia, sepsis, renal insufficiency, cardiac surgery with cardiopulmonary bypass, and specific calcium-avid cardiac diagnoses.

# METHODS

The study is a secondary analysis of the ICU-RESUScitation (ICU-RESUS) project.[10] Briefly, ICU-RESUS was a parallel, stepped-wedge hybrid cluster randomized trial comparing a CPR quality improvement bundle to usual care for its effect on survival outcomes. Eighteen paediatric (PICU) and paediatric cardiac ICUs (CICU) from 10 clinical sites in the U.S. participated between October 2016 and March 2021. The University of Utah Institutional Review Board (IRB) served as the central IRB and granted approval with waiver of consent.

ICU-RESUS included children ≥37 weeks post-conceptual age and ≤18 years who received chest compressions of any duration in an ICU. Exclusion criteria were (1) limitations to aggressive ICU therapies documented prior to cardiac arrest, (2) brain death, and (3) out-of-hospital cardiac arrest associated with the current hospital admission. For this secondary analysis, an additional exclusion criterion was use of extracorporeal membrane oxygenation (ECMO) at the start of CPR.

Trained research coordinators collected child and CPR event data consistent with the Utstein Resuscitation Registry Template for In-Hospital Cardiac Arrest.[11,12] Haemodynamic waveforms were collected from children with invasive arterial catheters and waveforms were analysed by investigators at The Children's Hospital of Philadelphia.[13,14]

Child data included demographics and pre-existing medical conditions. Pre-existing medical conditions included respiratory insufficiency, hypotension, congestive heart failure, pneumonia, sepsis, renal insufficiency, malignancy, trauma, and congenital heart disease. Specific calcium-avid cardiac diagnoses included interrupted aortic arch, tetralogy of Fallot, and truncus arteriosus due to their association with 22q11 deletion syndrome.[15]

Pre-event data included illness category, Paediatric Risk of Mortality (PRISM) score 2–6 hours prior to CPR,[16] vasoactive inotropic score (VIS) 2 hours prior to CPR,[17] highest serum potassium concentration, and hyperkalaemia (potassium ≥6 mmol/L) 2–6 hours prior to CPR. Event data included location of CPR (PICU or CICU), duration of CPR, date and time of CPR, first documented rhythm, immediate cause of cardiac arrest, interventions in place at start of CPR, open sternum at start of CPR, sternotomy performed during CPR, and pharmacologic interventions during CPR. Post-CPR event data included use of ECMO within 6 and 24 hours of CPR, and highest arterial lactate within 6 hours and between 6–24 hours, and highest pH within 6 hours.

Haemodynamic data included lowest systolic blood pressure 2–6 hours prior to CPR, average systolic and diastolic blood pressures one minute prior to CPR, average systolic and diastolic blood pressures over the first minute of CPR, and average systolic and diastolic

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blood pressures over the first ten minutes of CPR. Additional data included a diastolic blood pressure ≥25 mmHg for children <1 year of age, and ≥30 mmHg for children ≥1 year of age, and systolic blood pressure ≥60 mmHg for children <1 year of age, and ≥80 mmHg for children ≥1 year of age based on average measurements over the first one minute and ten minutes of CPR.[13]

Outcomes included sustained ROSC (>20 minutes), survival to hospital discharge, survival to hospital discharge with favourable neurologic outcome, and functional status at hospital discharge. Favourable neurologic outcome was based on the Paediatric Cerebral Performance Category (PCPC) and defined as PCPC score of 1 (normal), 2 (mild disability) or 3 (moderate disability), or no worse than baseline.[18] Functional outcome was based on the Functional Status Scale (FSS) and assessed in survivors as absolute change from baseline to hospital discharge.[19] New morbidity was defined as worsening from baseline FSS by 3 or more points.[19] Baseline PCPC and FSS represent the child's status prior to the event leading to hospitalization.

## Statistical Analysis

Child and event data were reported by calcium use (Tables 1 and 2). Categorical variables were summarized by counts and percentages, and continuous variables by medians, and first and third quartiles. Associations were assessed using Fisher's exact test for categorical variables, the Wilcoxon rank-sum test for continuous (interval) variables, and the Cochran-Armitage trend test for ordinal variables. Haemodynamic variables were similarly reported by calcium use and age (Table 3). Outcomes were summarized in a like manner but without statistical testing (Table 4) because further analysis was required to account for potential confounding factors.

To assess the effect of calcium use on outcomes, propensity weighted regression was used to reduce potential confounding from a priori factors.[20] This robust approach involves three main steps. First, a logistic regression model of calcium use was created to estimate each child's probability (propensity) for receiving calcium (Supplemental Material 1). Variables included in the model were study site, age, illness category, sepsis, PRISM, VIS, first documented rhythm, hypotension as the immediate cause of arrest, and CPR duration. A histogram of propensities was created for those with versus without calcium use (Supplemental Material 2).

Second, children were weighted using stabilized inverse probability of treatment weights. This weighting increases the balance of a priori characteristics between those with versus without calcium use, creating a weighted cohort in which children differ with respect to calcium use but are balanced with respect to potentially confounding characteristics (Supplemental Material 3). This is the mechanism by which confounding from characteristics is reduced. Thus, the level of balance obtained is critical. Differences in means and proportions were compared between those with versus without calcium use. When means between groups differed by less than one-tenth of a standard deviation, i.e. absolute standardized difference <0.10, the groups were considered well balanced.[20]

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Third, regression models were built using the weighted cohort to assess the effect of calcium use on outcomes (Table 5). Ordinary linear regression was used for continuous outcomes, and logistic regression was used for binary outcomes. These models controlled for four a priori selected variables (first documented rhythm, age, illness category, and CPR duration) to further reduce potential confounding from these variables and reduce the unexplained variability in the models to improve power.[21,22] Age was treated as categorical for modeling (≤1 month, >1 month - < 1 year, 1 year - < 8 years, 8 years - < 19 years).

Unweighted regression analysis was performed in pre-specified subgroups including neonates (≤1 month), children with hyperkalaemia, sepsis, renal insufficiency, cardiac surgery with cardiopulmonary bypass on the day of but prior to arrest, and calcium-avid cardiac diagnoses controlling for CPR duration (Supplemental Material 4–9). All analyses were performed using SAS 9.4 (SAS Institute; Cary, NC) with reported p-value based on a two-sided alternative and considered significant if less than 0.05.

## RESULTS

Of 1100 index CPR events, median child age was 0.63 years (IQR 0.19, 3.81) and 589 (53.5%) events were in males (Table 1). Calcium was used in 450 (41.0%) CPR events and was more common in children with pre-existing diagnoses of hypotension and congenital heart disease.

CPR event data are shown in Table 2. Calcium use was more common in surgical cardiac patients than medical cardiac or non-cardiac patients, and more common in CICU than PICU. Calcium was used more often in children with higher PRISM and VIS scores. Hyperkalaemia was present in 30 children; calcium was used in 20 (66%). Calcium use was associated with longer CPR duration, pulseless electrical activity (PEA) as the first documented rhythm, and hypotension as the immediate cause of arrest. Calcium use was associated with children having interventions in place at the start of CPR (central venous catheter, vasoactive infusion, invasive mechanical ventilation, open sternum), and having additional interventions provided during CPR (sternotomy procedure, other pharmacologic agents). Post-arrest characteristics associated with calcium use included higher arterial lactate and more ECMO cannulation within 6 hours of CPR and within 24 hours of CPR.

Haemodynamic data reported by calcium use and age are displayed in Table 3. Of 400 patients with arterial catheters, 191 (47.8%) received calcium. Fewer neonates treated with calcium achieved diastolic blood pressure ≥25 mmHg averaged over the first 1 minute of CPR. No other significant differences in haemodynamic measurements were observed between children who received calcium and those who did not in any age group.

Outcome data are reported in Table 4. Sustained ROSC was achieved in 216 (48.0%) children who received calcium versus 557 (85.7%) who did not. Survival to hospital discharge occurred in 189 (42.0%) children who received calcium versus 453 (69.7%) who did not, and survival with favourable neurologic outcome at hospital discharge occurred in 176 (39.1%) who received calcium versus 420 (64.6%) who did not. Among survivors

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(n=642), new morbidity occurred in 62 (32.8%) who received calcium versus 134 (29.6%) who did not.

Estimates of the effect of calcium use on outcomes among the weighted cohort are shown in Table 5. Calcium use was not associated with sustained ROSC but was associated with lower rates of survival to hospital discharge and survival with favourable neurologic outcome at hospital discharge. Calcium use was not associated with functional status or development of new morbidities in survivors.

Estimates of the effect of calcium on outcomes in subgroups are shown in Supplemental Material 4–9. Among neonates, children with hyperkalaemia, children with cardiac surgery on the day of IHCA, and children with calcium-avid cardiac diagnoses, calcium use was not significantly associated with any of the evaluated outcomes. In children with sepsis, calcium use was associated with lower rates of survival to hospital discharge and survival with favourable neurologic outcome at hospital discharge. In children with renal insufficiency, calcium use was associated with lower rate of survival to hospital discharge.

## DISCUSSION

In this propensity weighted multicentre cohort study of paediatric IHCA, we found that calcium was used frequently and that its use was associated with decreased rates of both survival to hospital discharge and survival with favourable neurologic outcome at hospital discharge. Worse outcomes with calcium use were observed even in some subgroups hypothesized to have potential to benefit from receiving calcium during CPR including children with sepsis and/or renal insufficiency. Calcium use was associated with cardiac surgery, greater illness severity, and longer duration of CPR. Calcium use was not associated with higher systolic or diastolic blood pressure during CPR.

Despite the AHA's limited indications for calcium use during paediatric IHCA,[3] calcium was used in 41% of events in our study. Srinivasan et al. reviewed 1477 paediatric index CPR events between 2000 and 2004 using data from the NRCPR and found calcium was used in 45% of events and associated with decreased rates of survival to hospital discharge and survival with favourable neurologic outcome at hospital discharge.[9] Similarly, Lasa et al used the AHA's Get with the Guidelines-Resuscitation (GWTG-R) registry to investigate outcomes of 203 paediatric CPR events occurring in the cardiac catheterization laboratory between 2005 and 2016.[6] Of these, calcium was used in 41% and associated with decreased rate of survival to hospital discharge. More recently, Dhillon et al used the GWTG-R registry to investigate outcomes of 4,556 children with heart disease experiencing an IHCA between 2000 and 2019.[5] Calcium was administered during CPR to 44% of children with heart disease and was associated with decreased rate of survival to hospital discharge. Our findings concur with those studies suggesting calcium is used frequently during paediatric IHCA and that its use is associated with worse outcomes.

Consistent with previous reports, we found calcium use was associated with greater severity of illness, longer duration of CPR and IHCA following cardiac surgery.[5,8,9] To account for these and other variables that may confound the relationships between calcium use

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and outcomes, our regression models were built using a propensity weighted cohort and additionally controlled for several a priori selected variables. Using this robust statistical approach, our results showed that calcium administration was associated with worse outcomes at hospital discharge. Unfortunately, the timing of calcium administration was not collected in the ICU-RESUS trial; therefore, we were unable to perform time-dependent propensity matching which further accounts for interventions that may be administered as a function of CPR duration.[23]

Although a randomized trial of calcium use during paediatric IHCA could provide more definitive conclusions about the effect of calcium on outcomes, no such trial in children has been conducted. In a recent double blind trial of adult out-of-hospital cardiac arrest by Vallentin et al., three hundred and ninety-one patients were randomized to receive calcium versus saline in addition to standard care.[24] The trial was stopped early due to concerns for harm in the calcium group. These authors concluded that treatment with calcium did not improve sustained ROSC among adults with out-of-hospital cardiac arrest, and reported trends for worse rates of survival and favourable neurologic outcome at 30 and 90 days. The mechanism behind the worse outcomes with calcium use may be related to increased intracellular calcium after myocardial and neuronal reperfusion.[25]

We evaluated haemodynamic characteristics of children in various age groups during the period immediately prior to CPR and during the first 10 minutes of CPR. The only significant finding was that neonates treated with calcium were less likely to achieve a target diastolic blood pressure ≥ 25 mmHg averaged over the first minute of CPR; a target previously shown to be associated with increased survival in this age group.[13] As the timing of calcium administration was not recorded in the ICU-RESUS study, we can only report that systolic and diastolic blood pressures were not greater in those that received calcium compared with those who did not.

We evaluated calcium use in subgroups considered most likely to benefit including neonates, and children with hyperkalaemia, sepsis, renal insufficiency, cardiac surgery with cardiopulmonary bypass, and specific calcium-avid cardiac diagnoses.[3, 15, 26–35] Neonatal myocardium has an underdeveloped sarcoplasmic reticulum and greater dependence on extracellular calcium sources then mature cardiac muscle. Calcium administration in neonates with low cardiac output can increase both heart rate and contractility.[26–29] However, we found no association between calcium use and outcomes among neonates in our study.

Calcium administration in children with hyperkalaemia is recommended to stabilize the myocardial membrane by restoring the altered transmembrane voltage gradient induced by hyperkalaemia.[3,4,30] We found no difference in outcomes for children with hyperkalaemia treated with calcium, although the number of hyperkalaemic children was small.

Hypocalcaemia is common during sepsis and has been associated with development of shock, multiple organ failure and mortality.[31,32] Although serum calcium concentrations were not collected in ICU-RESUS, children who received calcium for sepsis-related IHCA had decreased rates of survival to hospital discharge and survival with favourable neurologic

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outcome at hospital discharge. Hypocalcaemia and hyperkalaemia are also common in children with renal insufficiency.[33] Children with renal insufficiency receiving calcium during CPR had decreased rate of survival to hospital discharge.

Additionally, we evaluated children with cardiac surgery and cardiopulmonary bypass on the day of arrest because this subgroup is at risk for electrolyte imbalance due to blood product administration and other intra- and post-operative factors.[34,35] We also evaluated children with congenital cardiac lesions (interrupted aortic arch, tetralogy of Fallot, and truncus arteriosus) that are commonly associated with 22q11 deletion syndrome and hypocalcaemia.[15] We found no difference in outcomes among children with cardiac surgery or calcium-avid cardiac diagnoses with or without calcium use.

Strengths of this study include the multicentre design, prospective data collection, and use of a propensity weighted cohort to reduce the influence of potential confounding variables on outcomes. Limitations include lack of data regarding the timing of calcium administration precluding time-dependent analyses. Laboratory data were collected 2–6 hours prior to the CPR event and may not reflect intra-arrest values. Importantly, serum calcium concentrations were not recorded in the ICU-RESUS database nor were indications for calcium use. Only a third of children had arterial catheters to allow haemodynamic waveforms to be collected and analysed. Survival and survival with favourable neurologic outcome were assessed at time of hospital discharge, which is both variable and less important than long term outcomes. Importantly, this is an observational study and the associations described do not infer causation.

## CONCLUSIONS

In this propensity weighted multicentre cohort study of paediatric IHCA, calcium was used in 41% of CPR events and was associated with lower rates of both survival to hospital discharge and survival with favourable neurologic outcome at hospital discharge. Among subgroups, children with renal insufficiency and sepsis had worse outcomes with calcium use during IHCA.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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This work is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, or National Institutes of Health.

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**Table 1.**

Child Characteristics by Calcium Use

| | Calcium use | | |
|---|---|---|---|
| | No (N = 650) | Yes (N = 450) | P-value |
| **Demographics** | | | |
| Age | | | 0.010[1] |
| ≤ 1 month | 88 (13.5%) | 85 (18.9%) | |
| >1 month - < 1 year | 287 (44.2%) | 177 (39.3%) | |
| 1 year - < 8 years | 168 (25.8%) | 95 (21.1%) | |
| 8 years - < 19 years | 107 (16.5%) | 93 (20.7%) | |
| Male | 346 (53.2%) | 243 (54.0%) | 0.806[1] |
| Race | | | 0.160[1] |
| White | 292 (44.9%) | 224 (49.8%) | |
| Black or African American | 177 (27.2%) | 104 (23.1%) | |
| Other | 42 (6.5%) | 24 (5.3%) | |
| Unknown or Not Reported | 139 (21.4%) | 98 (21.8%) | |
| Hispanic or Latino | 104 (16.0%) | 60 (13.3%) | 0.339[1] |
| Weight (kg) | 7.1 [4.0, 14.7] | 7.0 [4.0, 18.0] | 0.618[2] |
| **Pre-existing medical conditions** | | | |
| Respiratory insufficiency | 574 (88.3%) | 371 (82.4%) | 0.008[1] |
| Hypotension | 353 (54.3%) | 340 (75.6%) | <.001[1] |
| Congestive heart failure | 74 (11.4%) | 66 (14.7%) | 0.118[1] |
| Pneumonia | 95 (14.6%) | 39 (8.7%) | 0.004[1] |
| Sepsis | 100 (15.4%) | 78 (17.3%) | 0.406[1] |
| Renal insufficiency | 78 (12.0%) | 67 (14.9%) | 0.174[1] |
| Malignancy | 26 (4.0%) | 25 (5.6%) | 0.245[1] |
| Trauma | 16 (2.5%) | 18 (4.0%) | 0.159[1] |
| Congenital heart disease | 350 (53.8%) | 282 (62.7%) | 0.004[1] |
| Calcium-avid cardiac diagnoses | 58 (8.9%) | 46 (10.2%) | 0.466[1] |
| Interrupted aortic arch | 8 (1.2%) | 8 (1.8%) | 0.456[1] |
| Tetralogy of Fallot | 43 (6.6%) | 33 (7.3%) | 0.717[1] |
| Truncus arteriosus | 8 (1.2%) | 8 (1.8%) | 0.456[1] |

[1] Fisher's exact test

[2] Wilcoxon rank-sum test

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**Table 2.**

Event Characteristics by Calcium Use

| | Calcium use | | |
|---|---|---|---|
| | **No (N = 650)** | **Yes (N = 450)** | **P-value** |
| **Pre-event characteristics** | | | |
| Illness category | | | 0.002[2] |
| Medical cardiac | 161 (24.8%) | 106 (23.6%) | |
| Surgical cardiac | 193 (29.7%) | 178 (39.6%) | |
| Non-cardiac | 296 (45.5%) | 166 (36.9%) | |
| Baseline PCPC score[1] | | | 0.067[4] |
| 1 - Normal | 375 (57.7%) | 294 (65.3%) | |
| 2 - Mild disability | 127 (19.5%) | 70 (15.6%) | |
| 3 - Moderate disability | 77 (11.8%) | 38 (8.4%) | |
| 4 - Severe disability | 63 (9.7%) | 44 (9.8%) | |
| 5 - Coma/vegetative state | 8 (1.2%) | 4 (0.9%) | |
| Baseline FSS[1] | 7.0 [6.0, 11.0] | 6.0 [6.0, 9.0] | 0.005[3] |
| Vasoactive inotropic score 2 hours prior to the event | | | <.001[3] |
| None | 425 (65.4%) | 214 (47.6%) | |
| 0 – 20 | 188 (28.9%) | 184 (40.9%) | |
| > 20 | 37 (5.7%) | 52 (11.6%) | |
| PRISM 2 – 6 hours prior to the event | 3.0 [0.0, 8.0] | 6.0 [1.0, 12.0] | <.001[3] |
| Glasgow Coma Scale | 11.0 [5.0, 14.0] | 11.0 [3.0, 14.0] | 0.463[3] |
| Highest serum potassium (mmol/L) | 3.9 [3.4, 4.5] | 3.9 [3.3, 4.7] | 0.870[3] |
| Hyperkalaemia (potassium ≥6 mmol/L prior to the CPR event) | 10 (1.5%) | 20 (4.4%) | 0.057[2] |
| **Event characteristics** | | | |
| Location of CPR Event | | | 0.005[2] |
| PICU | 339 (52.2%) | 195 (43.3%) | |
| CICU | 311 (47.8%) | 255 (56.7%) | |
| Duration of CPR (minutes) | 3.0 [1.0, 7.0] | 21.0 [9.0, 45.0] | <.001[3] |
| Duration of CPR (minutes) | | | <.001[2] |
| <6 | 439 (67.5%) | 67 (14.9%) | |
| 6–15 | 116 (17.8%) | 107 (23.8%) | |
| 16–35 | 58 (8.9%) | 126 (28.0%) | |
| >35 | 37 (5.7%) | 150 (33.3%) | |
| CPR time[5] | | | 0.395[2] |
| Weekday | 337 (51.8%) | 246 (54.7%) | |
| Weeknight | 124 (19.1%) | 90 (20.0%) | |
| Weekend | 189 (29.1%) | 114 (25.3%) | |

| | Calcium use | | |
|---|---|---|---|
| | No (N = 650) | Yes (N = 450) | P-value |
| First documented rhythm | | | 0.002[2] |
| Asystole | 73 (11.2%) | 48 (10.7%) | |
| Bradycardia with pulses | 365 (56.2%) | 203 (45.1%) | |
| Pulseless electrical activity | 162 (24.9%) | 157 (34.9%) | |
| Ventricular fibrillation | 15 (2.3%) | 17 (3.8%) | |
| Ventricular tachycardia | 35 (5.4%) | 25 (5.6%) | |
| Immediate cause | | | |
| Hypotension | 278 (42.8%) | 311 (69.1%) | <.001[2] |
| Respiratory decompensation | 393 (60.5%) | 204 (45.3%) | <.001[2] |
| Cyanosis without respiratory decompensation | 29 (4.5%) | 20 (4.4%) | 1.000[2] |
| Arrhythmia | 102 (15.7%) | 91 (20.2%) | 0.053[2] |
| Interventions in place | | | |
| Central venous catheter | 419 (64.5%) | 331 (73.6%) | 0.002[2] |
| Vasoactive infusion | 275 (42.3%) | 292 (64.9%) | <.001[2] |
| Invasive mechanical ventilation | 429 (66.0%) | 347 (77.1%) | <.001[2] |
| Non-invasive ventilation | 131 (20.2%) | 70 (15.6%) | 0.057[2] |
| Sternum open at start of CPR event | 46 (7.1%) | 60 (13.3%) | <.001[2] |
| Sternum opened during CPR event | 12 (1.8%) | 39 (8.7%) | <.001[2] |
| Pharmacologic interventions during CPR | | | |
| Adrenaline (Epinephrine) | 425 (65.4%) | 447 (99.3%) | <.001[2] |
| Adrenaline bolus administered in ≤ 5 minutes | 405/425 (95.3%) | 414/447 (92.6%) | 0.119[2] |
| Atropine | 62 (9.5%) | 61 (13.6%) | 0.041[2] |
| Sodium bicarbonate | 148 (22.8%) | 380 (84.4%) | <.001[2] |
| Vasopressin | 6 (0.9%) | 35 (7.8%) | <.001[2] |
| Amiodarone | 11 (1.7%) | 29 (6.4%) | <.001[2] |
| Lidocaine | 16 (2.5%) | 29 (6.4%) | 0.002[2] |
| Fluid bolus | 91 (14.0%) | 192 (42.7%) | <.001[2] |
| **Post-CPR characteristics** | | | |
| ECMO within 6-hours[6] | 37/592 (6.3%) | 34/305 (11.1%) | 0.013[2] |
| ECMO within 24-hours[6] | 47/592 (7.9%) | 45/305 (14.8%) | <.001[2] |
| Highest arterial lactate (mmol/L) (0 – 6 hours) | 5.4 [2.2, 10.2] | 10.3 [5.7, 16.1] | <.001[3] |
| Highest arterial lactate (mmol/L) (6 – 24 hours) | 2.3 [1.3, 5.1] | 4.1 [2.2, 8.5] | <.001[3] |

PCPC = Pediatric Cerebral Performance Category; FSS = functional status scale; PRISM = Pediatric Risk of Mortality; CPR = cardiopulmonary resuscitation; PICU = pediatric intensive care unit; CICU = cardiac intensive care unit; ECMO = extracorporeal membrane oxygenation.



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[1]Baseline PCPC and FSS represent the child's status prior to the event leading to hospitalization.

[2]Fisher's exact test.

[3]Wilcoxon rank-sum test.

[4]Cochran-Armitage test for trend.

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

[6]Denominator does not include those who transitioned to ECMO as their immediate outcome of CPR event.

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**Table 3.**

Haemodynamic Characteristics by Calcium Use

| | Calcium use | | |
|---|---|---|---|
| | No | Yes | P-value |
| **Age ≤ 1 month** | | | |
| Number with available arterial line data | 41 | 62 | |
| Lowest systolic pressure (mmHg) 2 – 6 hours prior to CPR | 61.5 [55.5, 69.5] | 61.0 [50.0, 67.0] | 0.430[1] |
| Average over 1 minute prior to CPR | | | |
| Diastolic pressure (mmHg) | 32.3 [23.6, 37.7] | 26.5 [19.6, 36.5] | 0.096[1] |
| Systolic pressure (mmHg) | 42.6 [37.3, 58.6] | 41.2 [30.6, 54.6] | 0.081[1] |
| Average over first minute of CPR | | | |
| Diastolic pressure ≥25 mmHg | 35 (87.5%) | 39 (65.0%) | 0.019[2] |
| Diastolic blood pressure (mmHg) | 32.0 [28.7, 42.8] | 30.2 [21.8, 39.1] | 0.100[1] |
| Systolic pressure ≥60 mmHg | 28 (71.8%) | 36 (61.0%) | 0.289[2] |
| Systolic blood pressure (mmHg) | 75.0 [58.5, 91.9] | 64.6 [53.3, 82.3] | 0.104[1] |
| Average over ten minutes of CPR | | | |
| Diastolic pressure ≥25 mmHg | 34 (82.9%) | 50 (80.6%) | 1.000[2] |
| Diastolic blood pressure (mmHg) | 33.9 [28.9, 42.8] | 30.9 [25.4, 39.5] | 0.224[1] |
| Systolic pressure ≥60 mmHg | 31 (77.5%) | 41 (67.2%) | 0.369[2] |
| Systolic blood pressure (mmHg) | 79.5 [62.0, 91.4] | 66.9 [54.6, 83.0] | 0.142[1] |
| **Age >1 month - < 1 year** | | | |
| Number with available arterial line data | 88 | 64 | |
| Lowest systolic pressure (mmHg) 2 – 6 hours prior to CPR | 74.0 [64.0, 83.0] | 72.0 [61.0, 82.0] | 0.310[1] |
| Average over 1 minute prior to CPR | | | |
| Diastolic pressure (mmHg) | 31.9 [26.4, 39.5] | 29.0 [23.5, 37.9] | 0.232[1] |
| Systolic pressure (mmHg) | 48.4 [38.3, 72.0] | 44.0 [36.3, 62.2] | 0.249[1] |
| Average over first minute of CPR | | | |
| Diastolic pressure ≥30 mmHg | 73 (83.9%) | 49 (76.6%) | 0.299[2] |
| Diastolic blood pressure (mmHg) | 36.2 [28.6, 45.3] | 30.7 [25.2, 43.4] | 0.053[1] |
| Systolic pressure ≥80 mmHg | 59 (68.6%) | 36 (56.3%) | 0.127[2] |
| Systolic blood pressure (mmHg) | 73.1 [55.2, 91.5] | 67.0 [50.8, 100.1] | 0.283[1] |
| Average over ten minutes of CPR | | | |
| Diastolic pressure ≥30 mmHg | 81 (92.0%) | 54 (84.4%) | 0.192[2] |
| Diastolic blood pressure (mmHg) | 39.0 [32.4, 51.9] | 35.4 [30.2, 48.6] | 0.170[1] |
| Systolic pressure ≥80 mmHg | 65 (74.7%) | 38 (59.4%) | 0.053[2] |

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| | Calcium use | | |
|---|---|---|---|
| | No | Yes | P-value |
| Systolic blood pressure (mmHg) | 78.8 [59.2, 93.6] | 71.7 [52.9, 100.4] | 0.272[1] |
| **Age 1 year - < 8 years** | | | |
| Number with available arterial line data | 46 | 32 | |
| Lowest systolic pressure (mmHg) 2 – 6 hours prior to CPR | 76.0 [70.0, 87.0] | 80.0 [63.0, 93.0] | 0.585[1] |
| Average over 1 minute prior to CPR | | | |
| Diastolic pressure (mmHg) | 30.6 [23.8, 39.3] | 31.0 [27.2, 42.7] | 0.902[1] |
| Systolic pressure (mmHg) | 46.9 [39.2, 66.0] | 53.1 [31.0, 63.6] | 0.790[1] |
| Average over first minute of CPR | | | |
| Diastolic pressure ≥30 mmHg | 33 (71.7%) | 22 (73.3%) | 1.000[2] |
| Diastolic blood pressure (mmHg) | 35.9 [28.4, 50.8] | 35.5 [27.9, 42.5] | 0.682[1] |
| Systolic pressure ≥80 mmHg | 21 (46.7%) | 12 (40.0%) | 0.639[2] |
| Systolic blood pressure (mmHg) | 71.6 [57.9, 103.7] | 77.3 [60.9, 90.9] | 0.607[1] |
| Average over ten minutes of CPR | | | |
| Diastolic pressure ≥30 mmHg | 41 (89.1%) | 24 (75.0%) | 0.127[2] |
| Diastolic blood pressure (mmHg) | 44.5 [37.7, 54.6] | 41.4 [29.4, 53.9] | 0.169[1] |
| Systolic pressure ≥80 mmHg | 31 (68.9%) | 20 (62.5%) | 0.629[2] |
| Systolic blood pressure (mmHg) | 94.5 [72.8, 115.3] | 84.1 [64.6, 98.5] | 0.085[1] |
| **Age 8 years - < 19 years** | | | |
| Number with available arterial line data | 34 | 33 | |
| Lowest systolic pressure (mmHg) 2 – 6 hours prior to CPR | 81.0 [69.0, 99.0] | 92.0 [71.0, 109.0] | 0.217[1] |
| Average over 1 minute prior to CPR | | | |
| Diastolic pressure (mmHg) | 34.2 [25.9, 42.7] | 28.1 [21.8, 43.3] | 0.376[1] |
| Systolic pressure (mmHg) | 47.0 [35.1, 72.9] | 41.2 [30.6, 63.8] | 0.300[1] |
| Average over first minute of CPR | | | |
| Diastolic pressure ≥30 mmHg | 26 (83.9%) | 24 (75.0%) | 0.536[2] |
| Diastolic blood pressure (mmHg) | 40.5 [33.6, 57.4] | 37.7 [29.2, 47.9] | 0.095[1] |
| Systolic pressure ≥80 mmHg | 19 (63.3%) | 16 (50.0%) | 0.317[2] |
| Systolic blood pressure (mmHg) | 101.5 [68.6, 129.9] | 80.3 [55.4, 110.6] | 0.137[1] |
| Average over ten minutes of CPR | | | |
| Diastolic pressure ≥30 mmHg | 30 (88.2%) | 28 (84.8%) | 0.734[2] |
| Diastolic blood pressure (mmHg) | 44.4 [34.6, 76.3] | 41.7 [34.1, 60.2] | 0.433[1] |
| Systolic pressure ≥80 mmHg | 25 (75.8%) | 22 (66.7%) | 0.587[2] |
| Systolic blood pressure (mmHg) | 104.0 [86.1, 138.2] | 114.3 [73.3, 133.9] | 0.617[1] |

CPR=cardiopulmonary resuscitation.

[1]Wilcoxon rank-sum test.

[2]Fisher's exact test.

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**Table 4.**

Summary of Outcomes by Calcium Use

| | Calcium use | | |
|---|---|---|---|
| | **No (N = 650)** | **Yes (N = 450)** | **Overall (N = 1100)** |
| Return of spontaneous circulation[1] | 557 (85.7%) | 216 (48.0%) | 773 (70.3%) |
| Survival to hospital discharge | 453 (69.7%) | 189 (42.0%) | 642 (58.4%) |
| Survival to hospital discharge with favourable neurologic outcome[2,3] | 420 (64.6%) | 176 (39.1%) | 596 (54.2%) |
| Survival to hospital discharge with PCPC of 1, 2, or no worse than baseline[2] | 385 (59.2%) | 160 (35.6%) | 545 (49.5%) |
| Change from baseline to hospital discharge in functional status of survivors[2] | 1.0 [0.0, 3.0] | 2.0 [0.0, 3.0] | 1.0 [0.0, 3.0] |
| New morbidity among survivors[4] | 134/453 (29.6%) | 62/189 (32.8%) | 196/642 (30.5%) |

[1] Return of spontaneous circulation reported is the immediate outcome of the resuscitation event.

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

[3] Favourable neurologic outcome is defined as Pediatric Cerebral Performance Category (PCPC) no more than moderate disability (PCPC of 1, 2, or 3) or no worse than baseline.

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

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**Table 5.**

Estimated Effect of Calcium Use on Outcomes

| Outcome | Adjusted odds ratio (95% CI) | Adjusted effect (95% CI) | P-value |
|---|---|---|---|
| Return of spontaneous circulation[1] | 0.87 (0.61, 1.24) | | 0.445 |
| Survival to hospital discharge | 0.68 (0.52, 0.89) | | 0.005 |
| Survival to hospital discharge with favourable neurologic outcome[2,3] | 0.75 (0.57, 0.98) | | 0.038 |
| Survival to hospital discharge with PCPC of 1, 2, or no worse than baseline[2] | 0.77 (0.59, 1.01) | | 0.060 |
| Change from baseline to hospital discharge in functional status (FSS) of survivors[2] | | 0.02 (−0.57, 0.61) | 0.942 |
| New morbidity (survivors only)[4] | 0.95 (0.63, 1.42) | | 0.792 |

Models were weighted using stabilized inverse probability of treatment weights and additionally controlled for first documented rhythm, age, illness category, and duration of CPR.

[1] Return of spontaneous circulation reported is the immediate outcome of the resuscitation event.

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

[3] Favourable neurologic outcome is defined as Pediatric Cerebral Performance Category (PCPC) no more than moderate disability (PCPC of 1, 2, or 3) or no worse than baseline.

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