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Resuscitation

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Clinical paper

Association of chest compression pause duration prior to E-CPR cannulation with cardiac arrest survival outcomes

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Abstract

Objective: To characterize chest compression (CC) pause duration during the last 5 minutes of pediatric cardiopulmonary resuscitation (CPR) prior to extracorporeal-CPR (E-CPR) cannulation and the association with survival outcomes.

Methods: Cohort study from a resuscitation quality collaborative including pediatric E-CPR cardiac arrest events $\geq$ 10 min with CPR quality data. We characterized CC interruptions during the last 5 min of defibrillator-electrode recorded CPR (prior to cannulation) and assessed the association between the longest CC pause duration and survival outcomes using multivariable logistic regression.

Results: Of 49 E-CPR events, median age was 2.0 [Q1, Q3: 0.6, 6.6] years, 55% (27/49) survived to hospital discharge and 18/49 (37%) with favorable neurological outcome. Median duration of CPR was 51 [43, 69] min. During the last 5 min of recorded CPR prior to cannulation, median duration of the longest CC pause was 14.0 [6.3, 29.4] sec: 66% >10 sec, 25% >29 sec, 14% >60 sec, and longest pause 168 sec. Following planned adjustment for known confounders of age and CPR duration, each 5-sec increase in longest CC pause duration was associated with lower odds of survival to hospital discharge [adjusted OR 0.89, 95 %CI: 0.79–0.99] and lower odds of survival with favorable neurological outcome [adjusted OR 0.77, 95 % CI: 0.60–0.98].

Conclusions: Long CC pauses were common during the last 5 min of recorded CPR prior to E-CPR cannulation. Following adjustment for age and CPR duration, each 5-second incremental increase in longest CC pause duration was associated with significantly decreased rates of survival and favorable neurological outcome.

Keywords: Cardiopulmonary resuscitation, Extracorporeal circulation, In-hospital cardiac arrest, Survival, Chest compression pauses, Pediatrics

Introduction

More than 290,000 adults and 15,000 children experience an in-hospital cardiac arrest (IHCA) each year in the United States.[1] Survival to hospital discharge occurs in about 22–52% of children impacted by multiple patient and event factors including high-quality chest compressions (CC), age of patient, and duration of cardiopulmonary resuscitation (CPR).[2–6] Longer pauses in CCs are associated with lower rates of survival in adults.[7–10] Accordingly, international guidelines recommend reducing duration of CC pauses to less than 10 seconds.[3,4]

In selected circumstances, when conventional CPR is unable to restore spontaneous circulation, extracorporeal CPR (E-CPR) may

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https://doi.org/10.1016/j.resuscitation.2022.05.004

Received 3 March 2022; Received in Revised form 27 April 2022; Accepted 5 May 2022

be attempted. E-CPR rescue following refractory pediatric IHCA, when compared to continued conventional CPR, has been associated with improved survival outcomes in some,[11,12] but not all studies.[13,14] A possible unstudied explanation for this variability in survival outcomes could be variable duration of CC pauses (i.e. "no flow time" for heart and brain) during E-CPR cannulation. The cannulation of peripheral and/or central vascular structures is the penultimate step in the process of initiating E-CPR, often with the surgeon requesting pauses in CC to facilitate cannulation. Due to technical challenges and diminutive vascular anatomy in the pediatric population, these interruptions in CC in the last minutes could be particularly long and potentially impactful on survival and neurological outcomes. A survey among pediatric critical care specialists revealed that the vast majority self-report long pauses in CC during E-CPR cannulation.[15] However, the actual duration of CC pauses during E-CPR cannulation and their association with survival outcomes has not been characterized.

This study aimed to 1) characterize CC pauses during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation, and 2) to evaluate the association of CC pause duration during this critical time period with survival and favorable neurologic outcomes. We hypothesized that the duration of the longest pause in CC in the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation would be associated with lower rates of survival to hospital discharge and favorable neurologic outcome.

Methods

This is a multicenter, multinational observational cohort study including data reported to the Pediatric Resuscitation Quality (pediRES-Q) Network. The pediRES-Q Collaborative (ClinicalTrials.gov, NCT02708134) is a pediatric resuscitation quality improvement network, previously described in detail.(15) The collection, management and analysis of data in this study (IRB # 15–12099) was approved by the Children's Hospital of Philadelphia institutional review board (IRB) (Federal Wide Assurance Identifier: FWA00000459) and determined that the study met criteria for a waiver of consent per Code of Federal Regulations 45 CFR 46.116(d) and 45 CFR 46.408(a). Sites participating in the collaborative were approved by their local IRB or research ethics boards and a Data Use Agreement was obtained.

Cohort selection

This study included data from July 2015 to December 2019 on all pediatric IHCAs in which E-CPR cannulation was reported to the pediRES-Q registry. We included data on index (first in-hospital) events from all children $\geq$ 37 weeks gestation and < 18 years of age who received external CC with pauses recorded by ZOLL R-series defibrillator electrode pads (ZOLL Medical, Chelmsford, Massachusetts, USA) and transmitted to the data coordinating center for secondary manual confirmation of pause duration. To exclude cases where extracorporeal membrane oxygenation (ECMO) vascular cannulation was initiated prior to CPR, we excluded all cases with CPR for < 10 minutes. As CC pauses are usually most prevalent during the last minutes of the E-CPR cannulation attempt, we chose to analyze data on the last 5 minutes of defibrillator electrode-pad recorded CPR. We sought to analyze CPR data as close to successful ECMO cannulation (ie. end of CPR) as feasibly possible, and thus prospectively selected the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation as our capture window. All pauses > 30 secs were manually confirmed by investigators for any signs of spontaneous circulation, including ECG rhythm, end-tidal CO_2 ($ETCO_2$), pulse oximetry, blood pressure, and resuscitation medical record.

Outcomes of interest

Utstein and P-COSCA recommended survival to hospital discharge and pediatric cerebral performance category (PCPC) at hospital discharge[16,17] were the primary outcomes of interest. Consistent with prior publications, we prospectively defined survival to hospital discharge with favorable neurological outcome as PCPC $\leq$ 3 or no change from baseline.[18]

Exposures of interest

We prospectively defined the duration of the longest pause during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation as the primary exposure of interest, based on the hypothesis that single long pauses were more likely to be more harmful than multiple short pauses.[19] We also conducted a prospectively planned secondary sensitivity analysis of patients where the exposure of interest was defined by defibrillator electrode pads specifically confirmed to remain on the patient within the last 5 minutes *immediately preceding* E-CPR cannulation and initiation of ECMO flow. This was performed because defibrillator electrode pads collecting data on CPR quality may be removed from the patient before cannulation in some cases (e.g. chest cannulation, slippage or removal of pads). Further, we conducted prospectively planned secondary analyses to assess the association between survival outcomes where the exposures of interest were: 1) dichotomous variables of pause length > 30 secs, >60 secs, or > 120 secs during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation; and 2) CCF > 80% during the last 5 minutes of recorded CPR preceding E-CPR cannulation (as recommended by the American Heart Association).[20] In addition, we collected patient- and event characteristics from the pediRES-Q registry.

Data analysis

This is a historical cohort, and no sample size calculation was performed. Categorial variables are presented as numbers (percent) and continuous data are expressed as mean ± standard deviation (SD) for normally distributed data and median [quartile 1 (Q1); quartile 3(Q3)] for non-normally distributed data. Data were assessed for normality using histogram analyses and quantile–quantile plots. The associations between pause length and survival to hospital discharge and survival with favorable neurological outcome were reported using logistic regression analysis. For the primary endpoint of longest pause duration during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation, we calculated the odds ratio (OR) for survival for every 5-second incremental increase in the longest pause duration. We used directed acyclic graphs (i.e., causal diagrams) to identify potential confounders for the association between pause length and survival outcomes (Appendix 1). We anticipated that age and CPR duration would be true confounders (i.e., associated with both pause duration for cannulation and survival outcomes). Due to the limited sample size, we applied the confounders and each potentially biasing variable using sequential multivariate logistic regression models. Illness category was analyzed by comparing surgical cardiac illness category to all other illness categories. For the planned sensitivity analyses with dichotomous exposures, we adjusted for confounding using a propensity score. The propensity score was applied as a covariate in the logistic regression model and included the variables: age, illness category, and duration of CPR. All tests were two-sided and a p-value of < 0.05 was considered as statistically significant. All associations are reported as OR with 95% confidence intervals (95% CI). No adjustment for multiple comparisons was performed. Data were analyzed using Stata version 16.0 (StataCorp LLC, College Station, TX, USA).

Results

We identified 202 pediatric IHCA E-CPR events and included 49 events with defibrillator electrode-pad recorded data and a duration of > 10 min collected across 13 hospital sites. Patients had predominantly cardiac illness categories (62%) and 19% had shockable first documented cardiac arrest rhythms (Table 1). Overall, 55% survived to hospital discharge and 37% survived with favorable neurological outcome (67% of survivors had favorable neurological outcome).

The median duration of the longest pause during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation was 14.0 sec [Q1, Q3: 6.3, 29.4]. Of those, 66% were longer than 10 sec, 25% were longer than 29 sec, 14% were longer than 60 sec (Fig. 1), and the longest pause was 168 sec. Patient characteristics and distribution of pause durations for the secondary sensitivity analysis of cases with defibrillator electrode pads confirmed to remain on the patient within the last 5 minutes immediately preceding initiation of ECMO flow is shown in Appendix 2 and 3. Stratified by cannulation site, the longest pause in each CPR event was 11.6 sec [5.3, 35.7] for groin cannulations, 12.8 sec [7.5, 29.4] for cases with unknown/other site of cannulation, 15.0 sec [3.9–24.3] for neck cannulations, and 24.5 sec [12.0, 30.9] for chest cannulations. The median CCF during the last 5 min of defibrillator electrode pad recorded CPR was 85% [64%, 95%]. The number of events with any pause > 30 secs was 12 (24%), >60 secs was 7 (14%), and > 120 secs was 3 (6%).

After adjustment for a-priori defined confounders of age and CPR duration, each 5-sec increment increase in longest pause duration during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation was associated with lower survival to hospital discharge (aOR: 0.89, 95% CI: 0.79–0.99, p = 0.04) (Fig. 2A) and lower survival with favorable neurological outcome (aOR: 0.77, 95% CI: 0.60–0.98, p = 0.03) (Fig. 2B). These findings remained consistent across sequential multivariate logistic regression analyses adjusting for potentially biasing covariates including illness category, cannulation site, chest compression depth, and sex (Fig. 2).

For the planned secondary sensitivity analysis of patients with documented confirmation that electrode pads were in place within the last 5 minutes preceding initiation of ECMO flow (N = 28), point estimates were consistent for the association with survival to hospital discharge and survival with favorable neurological outcome (Appendix 4–5).

Overall, (2/7) patients (29%) with longest CC pause duration > 60 secs during the last 5 minutes of electrode-pad recorded CPR prior to E-CPR cannulation survived to hospital discharge. CCF > 80% nor any pauses > 30 secs, >60 secs, and > 120 secs during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation were *not* associated with survival to hospital discharge or survival with favorable neurological outcome (Table 2). The association between CCF > 80%, pauses > 30 secs, >60 secs, and > 120 secs with survival outcomes remained non-significant even after propensity score adjustment.

Discussion

This is the first study to report actual CC pause durations during CPR in the minutes preceding E-CPR cannulation and their association with survival outcomes. We were surprised to find that the median duration of the longest pause during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation was only 14 seconds. As expected, the majority of longest pauses were greater than 10 secs, 25% were longer than 29 seconds, and 14% were longer than 60 secs. Of importance, after adjustment for important known confounders, each 5-second incremental increase in the longest pause duration during the last 5 minutes of electrode pad recorded CPR preceding E-CPR cannulation was associated with significantly lower odds for survival to hospital discharge and favorable neurologic survival at hospital discharge. Overall, these findings provide the first quantitative evidence-based support for international resuscitation guidelines regarding minimizing CPR duration pauses during E-CPR cannulation in children.

Until now, a number of studies have investigated CC pauses during adult out-of-hospital cardiac arrest,[19,21,22] but less is known about causes for CC pauses during pediatric IHCA.[23,24] Our findings document for the first time that the majority of resuscitation attempts with E-CPR cannulations reported to a multicenter quality improve-

Table 1 – Patient demographics.

Patient characteristics	All patients (n = 49)
Sex (% female)	24 (49%)
Race	
- White	26 (53%)
- Black	10 (20%)
- Other	10 (20%)
- Unknown	3 (6%)
Age (years)	2.0 (0.6, 6.6)
CPR duration (minutes)	51 (43, 69)
Initial pulseless rhythm	
- VF/ VT	10 (21%)
- PEA	27 (56%)
- Asystole	8 (17%)
- Other/unknown	4 (8%)
Illness category	
- Medical cardiac	15 (31%)
- Surgical cardiac	15 (31%)
- Medical non-cardiac	13 (27%)
- Surgical non-cardiac	5 (10%)
Cannulation site	
- Neck	21 (47%)
- Chest	4 (9%)
- Groin	5 (11%)
- Other/unknown	15 (34%)

Table legends: Continuous data are reported as median [quartile 1; quartile 3] whereas binary data are reported as number (percent).

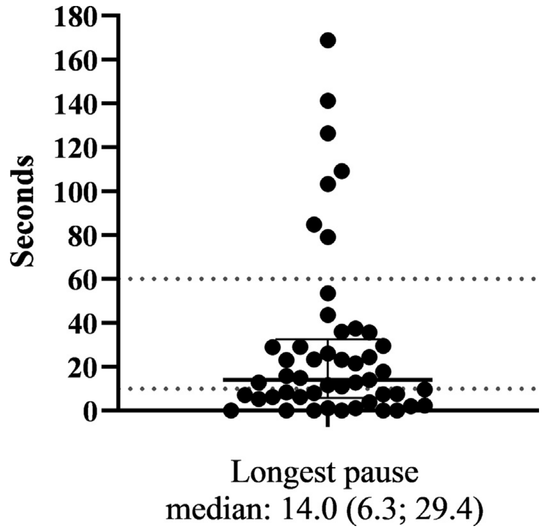

Fig. 1 – Longest pause duration during the last 5 min of defibrillator-electrode pad recorded CPR prior to E-CPR cannulation for each cardiac arrest event. Dotted lines represent 10-second pause length (maximum pause length recommended by the American Heart Association)[20] and 60-second pause length.

ment registry have pauses longer than 10 secs, despite AHA recommendations to avoid pauses > 10 seconds.[20] Our findings are consistent with a survey from Lasa et al. in which 77% of physicians self-reported > 10 second CC pauses during pediatric E-CPR cannulation.[15] However, we were surprised that the median longest pause duration was only 14 seconds for the technically challenging surgical procedure. This may reflect the heightened attention of the pediRES-Q quality-improvement collaborative, which audits and trains their sites using real-time feedback of quality metrics from defibrillators, minimization of CC pauses, and data-driven debriefing of events.[25] Notably, in some events, the longest pauses had a duration of only a few seconds. As we do not know what specifically happened during the pauses, it may be speculated that emphasis on minimizing pause duration in this Quality Improvement collaborative resulted in very short cannulation pauses, equivalent of pause duration for ventilations or switch of chest compressors.

Our finding that each incremental 5-second increase in the longest CC pause during the last 5 minutes of recorded CPR prior to E-CPR cannulation is significantly associated with lower rates of survival to hospital discharge and survival with favorable neurological outcome are novel and important. Although the findings are derived from a relatively small data set, the estimates were consistent across multivariable sequential analyses. In addition, the secondary sensitivity analyses of restrictive subsets of patients with confirmed documentation of electrode pads in place within the last 5 minutes immediately prior to ECMO circuit were also consistent although the confidence intervals were wider due to the smaller sample with less power. Studies that report an association between longer pause durations and lower survival rates have previously been from cohorts of adult out-of-hospital cardiac arrest patients with shockable rhythms.[7,19,26] Only a few prior studies have reported on the association between CCF and survival following pediatric cardiac arrest.[27,28] These studies did not find a positive association between CCF and survival following pediatric out-of-hospital cardiac arrest[27] or pediatric IHCA.[28] These prior studies did not analyze specifically for association with the longest pause duration and did not focus on CPR events that were refractory to conventional CPR. Moreover, our current study focuses on pauses during the last 5 minutes of defibrillator-electrode pad recorded CPR preceding E-CPR cannulation, instead of the first 10 minutes of CPR or the entire CPR event.[19].

Not surprisingly, we were unable to demonstrate associations between survival outcomes and CCF > 80% or specific dichotomous pause durations of > 30, >60, or > 120 seconds. This is likely because only very few patients had longer pauses of > 60 and > 120 sec during the last 5 minutes of recorded CPR, resulting in a very low power for the analysis. In support of that interpretation, our point estimate trends are consistent with the hypothesis that high CCF is associated with better survival outcomes, and longer pauses during the last 5 minutes of recorded CPR preceding E-CPR cannulation are associated with lower rates of survival and favorable neurologic outcome.

Similar to our study, an adult investigation of out-of-hospital VF arrest showed a statistically significant association between longest pause duration and survival, but not for CCF.[19] In addition, several other non-E-CPR studies have failed to show a significant association between CCF and survival following cardiac arrest, perhaps due to confounders such as CPR duration.[29–35] [36] Moreover, CPR

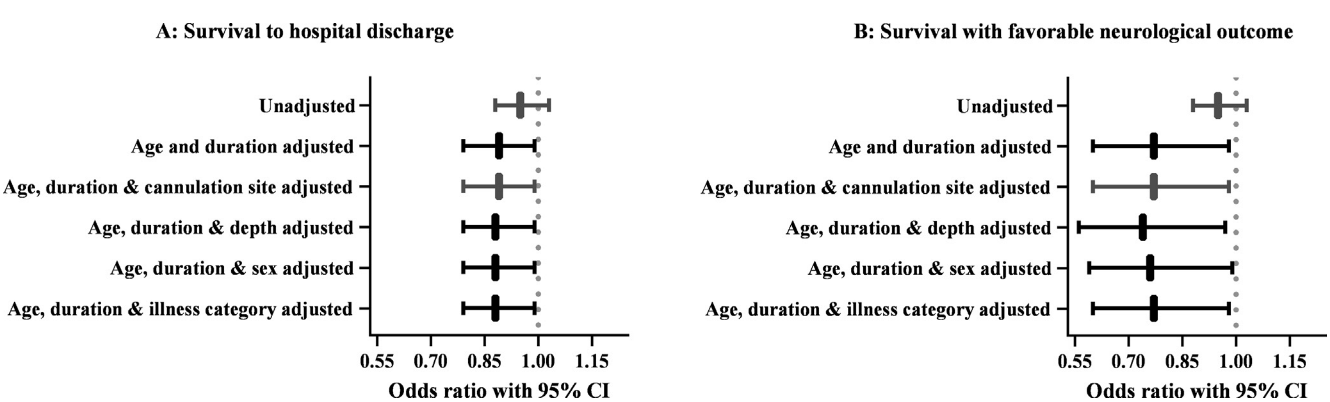

Fig. 2 – Odds ratio with 95% confidence intervals for the association between each 5-sec increment in the longest chest compression pause duration during the last 5 min of defibrillator-electrode pad recorded CPR prior to E-CPR cannulation and survival to hospital discharge (2a) and survival with favorable neurological outcome (2b).

Table 2 – Sensitivity analyses of association between chest compression pauses metrics and survival outcomes.

Sensitivity analysis	Unadjusted analyses		Propensity-adjusted analyses	
	Survival to hospital discharge	Favorable neurological outcome	Survival to hospital discharge	Favorable neurological outcome
CCF > 80%	1.42 (0.45–4.46)	2.44 (0.70–8.50)	1.54 (0.46–5.17)	1.97 (0.52–7.55)
Pauses > 30 sec	0.49 (0.13–1.83)	0.82 (0.21–3.24)	0.59 (0.14–2.37)	0.73 (0.17–3.12)
Pauses > 60 sec	0.27 (0.05–1.57)	0.24 (0.02–2.22)	0.45 (0.07–2.90)	0.50 (0.05–5.32)
Pauses > 120 sec	0.38 (0.03–4.55)	0.85 (0.72–10.12)	0.73 (0.04–13.45)	1.61 (0.09–29.86)

Table legends: Odds ratios with 95% confidence intervals for the associations between different metrics of chest compression pauses during the last 5 mins of defibrillator-electrode pad recorded CPR prior to E-CPR cannulation and survival to hospital discharge and survival to hospital discharge with favorable neurological outcome, with- and without adjustment. Adjustment was performed using propensity scores accounting for initial rhythm, cardiac illness category, CPR duration, and age.

duration is impacted by time to activation of the ECMO team and cannulation time, which may be associated with outcomes following E-CPR.[6,37] Thus, we pre-specified CPR duration and age as confounders using directed acyclic graphs (i.e., causal diagrams, Appendix 1). Notably, CCF is dependent on both short pauses (e.g. ventilations, pulse checks, etc.) and long pauses (e.g. ECMO cannulations), and we speculate that longer single durations of no-flow to the brain may be more detrimental than several shorter pauses. As our limited sample size precluded identification of any specific time cut-off for pause duration that was associated with worse survival outcomes, this important clinical question should be addressed in future studies.

In contrast to previously published pediatric and adult cohorts reporting on pauses in CC, the present study focuses only on the special resuscitation circumstance of prolonged resuscitation attempts (>10 minutes) evolving to E-CPR. Patient level factors such as illness category have been previously shown to be associated with survival in the E-CPR population, with improved survival for children with surgical cardiac conditions compared to medical cardiac and non-cardiac illness categories.[37,38] Given that almost a third of cases in our study were cardiac surgical illness category, we adjusted for this covariate and found no association or changes in the estimates. Although it is a subjective assessment by the clinician when a patient is refractory to CPR, patients in this cohort were presumably judged clinically to have potentially reversible conditions as rationale for activating E-CPR. Despite a common belief that interruption of CC for rapid initiation of ECMO flow to such patients is more important than minimizing interruptions in CC immediately prior to cannulation,[39] our findings suggest that specific attention should be given to the duration of interruptions in chest compressions immediately prior to E-CPR cannulation.

Limitations

The observational study design precludes determination of a causal effect. In addition, findings from this select cohort of critically ill children within a quality improvement collaborative with capability for E-CPR focused on high quality CPR may not be generalizable to other pediatric IHCA populations. The sample size was small and likely underpowered to show significant associations for some additional pause metrics association with survival outcomes. In addition, the sample size limited our ability to control for some covariates (e.g. hospital site), assess for potential mediation by interventions after ROSC, and precludes our ability to draw any strong conclusions. We do not have explicit data from additional potentially informative data sources (e.g. arterial waveforms, monitors other than the monitor-defibrillator, live-capture video) on what happened during each pause. Thus, some pauses might have been due to causes other than E-CPR cannulation. However, the longest pauses observed in this study were longer than what has been previously reported for rhythm check and defibrillation.[23,40] In addition, the defibrillator electrode-pads were removed within the last minutes leading up to E-CPR cannulation in some cases. Moreover, this study investigated the impact of CC specifically restricted to the last 5 minutes of defibrillator electrode-pad recorded CPR prior to E-CPR cannulation and may not reflect the impact of CC pauses during the earlier phases of CPR events.

Conclusions

In this observational study within a pediatric CPR quality collaborative, long CC pauses were common during the last 5 minutes of defibrillator-electrode pad recorded CPR prior to E-CPR cannulation. Following adjustment for age and CPR duration, each 5-second incremental increase in longest CC pause duration was associated with significantly decreased rates of survival and favorable neurological outcome, but no specific duration length cutoff was identified.

CRediT authorship contribution statement

Kasper G. Lauridsen: Conceptualization, Methodology, Investigation, Formal analysis, Project administration, Writing – original draft, Writing – review & editing. **Javier J. Lasa.** Investigation, Methodology, Writing – review & editing. **Tia T. Raymond:** Investigation, Methodology, Writing – review & editing. **Priscilla Yu:** Investigation, Methodology, Writing – review & editing. **Dana Niles:** Resources, Methodology, Project administration, Writing – review & editing. **Robert M. Sutton:** Investigation, Methodology, Writing – review & editing. **Ryan W. Morgan:** Investigation, Methodology, Writing – review & editing. **Mary Fran Hazinski:** Supervision, Methodology, Writing – review & editing. **Heather Griffis:** Formal analysis, Project administration, Writing – review & editing. **Richard Hanna:** Formal analysis, Project administration, Writing – review & editing. **Xuemei Zhang:** Formal analysis, Project administration, Writing – review & editing. **Robert A. Berg:** Methodology, Supervision, Writing – review & editing. **Vinay M. Nadkarni:** Conceptualization, Resources, Methodology, Investigation, Formal analysis, Project administration, Supervision, Writing – review & editing.

Acknowledgement

We would like to thank the clinicians and staff at all pediRES-Q sites for indispensable time and dedication to this collaborative effort.

Conflicts of interest

The authors declared no financial conflicts of interest. Kasper G. Lauridsen MD, PhD received funding by the AP Møller and Elite-Forsk by the Danish Ministry for Higher Education and Research. Vinay Nadkarni MD received unrestricted research funding to his institution from the National Institutes of Health, Agency for Healthcare Research and Quality, Zoll Medical, Nihon-Kohden Inc., and Volunteers on Scientific Advisory Committees for the American Heart Association, Citizen CPR Foundation, INSPIRE simulation research network, and Citizen CPR. Dana Niles MS disclosed that The Children's Hospital of Philadelphia receives support from an unrestricted research grant from ZOLL Medical. Dr. Morgan's effort on this work was supported by a National Institutes of Health Career Development Award from the National Heart, Lung, and Blood Institute ().

Funding

The pediRES-Q is supported by an unrestricted research grant to the Children's Hospital of Philadelphia from ZOLL Medical. The sponsor had no role in the design, interpretation, writing, editing, or submission of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2022.05.004.

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