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Cardiopulmonary resuscitation for in-hospital events in the emergency department: A comparison of adult and pediatric outcomes and care processes[☆]

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Abstract

Objectives—To compare outcomes from in-hospital cardiopulmonary resuscitation (CPR) in the emergency department (ED) for pediatric and adult patients and to identify factors associated with differences in outcomes between children and adults.

Methods—Retrospective analysis of the Get With The Guidelines – Resuscitation database from January 1, 2000 to September 30, 2010. All patients with CPR initiated in the ED requiring chest compressions for ≥ 2 min were eligible; trauma patients were excluded. Patients were divided into children (≤ 18 yo) and adults (> 18 yo). Patient, event, treatment, and hospital factors were analyzed for association with outcomes. Univariate analysis was performed comparing children and adults. Multivariate analysis was used to determine factors associated with outcomes.

Results—16,834 events occurred in 608 centers (16,245 adult, 537 pediatric). Adults had more frequent return of spontaneous circulation (53% vs 47%, $p = 0.02$), 24 h survival (35% vs 30%, $p = 0.02$), and survival to discharge (23% vs 20%, $p = \text{NS}$) than children. Children were less frequently monitored (62% vs 82%) or witnessed (79% vs 88%), had longer duration (24 m vs 17 m), more epinephrine doses (3 vs 2), and more frequent intubation attempts (64% vs 55%) than adults. There were no differences in time to compressions, vasopressor administration, or

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defibrillation between children and adults. On multivariate analysis, age had no association with outcomes.

Conclusions—Survival following CPR in the ED is similar for adults and children. While univariate differences exist between children and adults, neither age nor specific processes of care are independently associated with outcomes.

Keywords

Cardiopulmonary resuscitation; Emergency department; Pediatrics

1. Introduction

In-hospital cardiopulmonary resuscitation (CPR) has seen improving outcomes in both adult and pediatric patients over the past few decades. Among in-hospital locations where CPR is performed, the emergency department (ED) constitutes a minority of such events, comprising 9–11% of all in-hospital CPR events in both adult and pediatric patients.^{1–3} Outcomes among patients receiving CPR during an ED visit are likely influenced in a more complex manner by prehospital care, premorbid medical conditions, and variances in care processes that patients in other in-hospital settings. Few studies have exclusively examined this subset of patients.

Previously published studies from the American Heart Association Get With the Guidelines – Resuscitation registry (formerly the National Registry of Cardiopulmonary Resuscitation) on outcomes from CPR in the ED have yielded results that differ greatly between adult and pediatric patients. Children receiving CPR in the ED have been shown to have much poorer survival when compared to CPR outcomes in other in-hospital locations.^{1,4} Adults, by contrast, were found to be twice as likely to survive to hospital discharge when compared with events in the intensive care unit (ICU) or ward when analyzed within the same database.²

Reasons for the differences in outcomes between children and adults following CPR in the ED are not clear. The epidemiology and underlying physiology of cardiac arrest is significantly different between pediatric and adult patients, with children having a greater prevalence of respiratory and circulatory insufficiency as underlying causes leading up to cardiac arrest, as opposed to sudden cardiac death.⁵ It is possible that children arresting in the ED are in a more advanced state of acidosis, hypoxia, and metabolic deterioration at the time CPR is initiated. Additionally, pediatric cardiac arrest events are much less common than adult events. Even at tertiary pediatric centers, the incidence of cardiac arrests in the ED is very low^{1,4}; in non-pediatric EDs, where more than 90% of pediatric patients are initially managed, these events are even less common. It is possible that, as a result of infrequent clinical experience, care delivery to pediatric patients is less optimal during CPR, which may negatively influence outcomes.

With the present study, we sought to clarify factors that contributed to this marked discrepancy in the influence of ED as a location on CPR outcomes between adults and children. We performed an analysis of the American Heart Association Get With the

Guidelines – Resuscitation database examining outcomes following CPR in the ED among children and adults. We hypothesized that children would have worse survival outcomes than adults, and that we would identify significant factors related to patient, event, treatment, and hospitals that were independently associated with outcomes.

2. Methods

This was a retrospective cohort study of the Get With the Guidelines – Resuscitation database (GWTG-R, formerly the National Registry of Cardiopulmonary Resuscitation, or NRCPR), a multihospital registry of CPR events sponsored by the American Heart Association. Hospitals voluntarily participate in the database for the primary purpose of quality improvement and as such are not required to obtain institutional review board approval or informed consent from patients or families. The study was exempted from oversight by the Institutional Review Board of the Children’s Hospital of Philadelphia.

Hospitals participating in the registry submit clinical information regarding the medical history, hospital care, and outcomes of consecutive patients hospitalized for cardiac arrest using an online, interactive case report form and Patient Management Tool (Outcome, A Quintiles Company, Cambridge, MA). Outcome, A Quintiles Company, serves as the data collection (through their Patient Management Tool – PMT) and coordination center for GWTG. The University of Pennsylvania serves as the data analytic center and has an agreement to prepare the data for research purposes.

According to operational definitions for the GWTG-R database, a patient is eligible for enrollment if they experience a clinical event marked by either cardiac arrest or critical bradycardia and/or hypoperfusion treated with chest compressions, and leading to a unit-wide or hospital-wide systematic response. Patients whose clinical event treated with chest compressions begins out-of-hospital and is then continued on arrival to the hospital are excluded. Newly born infants receiving chest compressions in the delivery room are excluded.

For the current study, data on events occurring at enrolling hospital between January 1, 2000 and September 30, 2010 were examined. All patients receiving chest compressions for >2 min initiated in the emergency department were eligible for inclusion. Trauma patients, patients whose event was not an index event (i.e. the first CPR event during a given hospital stay), and patients whose age was listed as unknown were excluded.

A list of patient, event, hospital, and treatment characteristics likely to be significant confounders and/or effect modifiers was developed a priori by investigator consensus (Fig. 1). These factors and their definitions were derived from prior published analyses of the GWTG-R/NRCPR where they were found to have significant associations with outcomes.^{3,4,6,7} Event duration was defined as the time interval from the delivery of the first chest compression until either the time of sustained ROSC (lasting >20 min) or the time when resuscitation efforts were terminated. Weekend events were defined as events occurring during the time interval from 5:00 PM Friday to 6:59 AM Monday. Respiratory support was defined as the presence of one or more of the following: assisted ventilation,

mechanical ventilation, or inhaled nitric oxide. Cardiovascular support was defined as the presence of any vasoactive infusion and/or any antiarrhythmic infusion. Monitored was defined as presence of one or more of the following: ECG, pulse oximetry, or apnea monitor. Shockable rhythm was defined as an event with a first documented rhythm of pulseless ventricular tachycardia or ventricular fibrillation. CPR for bradycardia was defined as being present if the initial rhythm was bradycardia and the initial pulse status was labeled as 'pulse present'. Subsequent VF was defined as an event where the initial rhythm was not shockable (asystole, PEA, bradycardia) but VF/pVT occurred at some point. Advanced airway management was defined in one of three categories: advanced airway already in place, airway placement attempted during the event, or no attempt at airway placement during the event.

Pediatric patients were defined as patients aged less than 18 years; all other patients were classified as adults. Hospitals were classified as 'pediatric', 'adult', or 'mixed' by self-report in the database; this data field was collapsed into a dichotomous category of pediatric hospitals and non-pediatric hospitals (Fig. 2).

2.1. Outcome measures

Prospectively determined outcomes of interest were return of spontaneous circulation (ROSC), 24 h survival, and survival to hospital discharge; these were defined according to Utstein definitions.⁸ Patients with unknown or missing 24 h survival status were excluded from analysis for both 24 h survival and survival to discharge.

2.2. Data analysis

All variables were summarized descriptively. Univariate analysis between pediatric and adult patients for Utstein outcomes and for each patient, event, and treatment characteristic was performed using chi square analysis for categorical variables and nonparametric (Wilcoxon rank-sum) testing for continuous variables.

Multivariable logistic regression models were used to examine the effect of our primary exposure group on survival outcomes. These models were fit as generalized estimating equations to account for within-facility covariance. Prospectively designated potential confounders were included as candidate predictors in the models. For each outcome, a final multivariable model was fit to include the covariates determined to be significant at $\alpha = .10$ in the initial model. Patient age (pediatric versus adult) was included in all final models.

3. Results

Of 200,602 events requiring CPR at 608 hospitals during the study period, 16,782 (8%) occurred in the emergency department. 16,245/189,654 (8.6%) of adult events and 537/10,948 (5%) of pediatric events were initiated in the ED. 52 patients (<1%) were excluded due to missing data on outcomes or age. 66/537 (12%) of pediatric patients and 594/16,245 (4%) of adult patients had missing or incomplete data on 24 h survival and were excluded from analysis of 24 h survival and survival to discharge.

A diagram summarizing outcomes stratified by age group (pediatric versus adult) following the standard Utstein template for cardiac arrest reporting is shown in Fig. 3.⁸ Unadjusted univariate analysis of outcomes between pediatric and adult patients showed a higher rate of ROSC ($p = 0.02$) and 24 h survival ($p = 0.02$) in adult patients; we found no significant difference in survival to discharge between pediatric and adult patients.

A summary of the patient and event characteristics among pediatric and adult patients is shown in Table 1. Univariate comparison between adult and pediatric patients showed higher rates of shockable rhythms and subsequent VF/pVT among adults, lower rates of monitored and witnessed status among children, and a higher prevalence of CPR for bradycardia among children. Pre-event cardiovascular support was more common among adults and pre-event respiratory support was more common among children.

Treatment variables by patient group are summarized in Table 2. Pediatric patients had longer event duration, great number of epinephrine doses, higher incidence of attempted invasive airway placement during the event, and a lower prevalence of event ending without any attempted airway placement.

Multivariate analysis results for the entire cohort are shown in Table 3. Factors positively associated with all survival outcomes included shockable rhythm and the absence of attempted advanced airway placement. Factors negatively associated with all outcomes included ED volume of less than 4000 visits per year, pre-existing cardiovascular support, hypotension as immediate cause, increasing number of epinephrine doses, and increased duration. Age category (pediatric versus adult) was not significantly associated with survival. No time interval related to specific interventions had a univariate association with any outcome that led to inclusion in the final multivariate model.

4. Discussion

In our study, we demonstrated that survival from cardiac arrest in the emergency department was not significantly different between adults and children when controlled for important patient, event, hospital, and clinical factors. Unadjusted comparison between children and adults demonstrated lower incidence of ROSC and 24 h survival among pediatric patients; however, this association did not remain significant in multivariate analysis. Important differences between pediatric and adult patients were found in univariate analysis with respect to patient, event, and treatment factors. However, age category was not significantly associated with survival outcomes.

While we hypothesized that discrepancies in fundamental care processes might account for differences in outcomes between children and adults, we found no significant differences in times to chest compressions, defibrillation, or epinephrine administration between pediatric patients and adult patients. When controlled for in our analysis, these objective measures of care delivery had no significant association with survival.

The vast majority of pediatric CPR events in the ED are patients suffering out-of-hospital cardiac arrest whose resuscitation is continued on arrival to the ED. Survival from in-hospital cardiac arrest of children has improved substantially in the past few decades, from

survival rates of 10% in the 1980s to greater than 25% in 2005.^{3,9,10} At the same time, survival from out-of-hospital cardiac arrest in children has changed very little in the past 30 years, with survival rates of less than 10% in virtually all published studies.^{11–13} In the first descriptive study to summarize outcomes among pediatric patients with non-traumatic cardiac arrest while in a children's hospital ED, Teach and colleagues showed an overall survival rate of 19%, higher than out-of-hospital cardiac arrest survival rates for children but less favorable than in-hospital cardiac arrest.¹⁴ Subsequent controlled studies from the NRCPR/GWTG-R database, which included trauma patients, demonstrated a negative association with survival among children suffering CPA in the ED.¹ In the present study of non-traumatic cardiac arrest, while we found an overall survival of 20% in pediatric patients, survival among patients in pediatric hospital EDs was 28%, suggesting improvement in survival among cardiac arrest patients in pediatric EDs when compared with previous reports from decades ago.

In an earlier evaluation of GWTG-R data, Kayser et al. found that the ED location of adult cardiac arrest events was associated with improved survival to discharge compared with arrest events in the ICU or ward location.² In a recent investigation of ED cardiac arrest resuscitations, hospital-level variables were associated with improved outcome, including teaching hospital status and the capability to perform percutaneous coronary interventions.¹⁵ Similar data in post-arrest care for children do not presently exist, and the current recommendations from the American Heart Association for pediatric post-arrest care are very limited in terms of specific care recommendations, focusing instead of the regionalization of care of such patients in tertiary pediatric ICUs.¹⁶ As mentioned above, 66 pediatric patients (12%) had missing data on 24 h survival and were coded as 'discharged alive', suggesting that they were transferred to other centers for post-arrest care; only one of these 66 patients had their index event at a pediatric center. Given the fact that 71% of the pediatric events occurred in the EDs of non-pediatric hospitals, these data suggest that children who achieve ROSC following cardiac arrest in the ED are not transferred to tertiary pediatric critical care centers at an optimal frequency.

We found that patients with an invasive airway in place had worse survival than patients who had attempted insertion or reinsertion of an invasive airway during their CPR event. Additionally, patients who had no attempt at invasive airway placement during their event had significantly improved survival; importantly, this association remained significant while controlling for event duration. A recent consensus statement from the American Heart Association summarized available evidence regarding advanced airway placement in the arrested patient, emphasizing the need to minimize the duration of interruptions in compressions occurring due to airway management.¹⁷ We may infer from our data that patients with no attempted airway placement benefited from a lack of CPR interruption for intubation; quantifying the interruptions in CPR is not possible from the current database. An additional explanation for this finding may be that patients whose immediate post-arrest recovery was more robust (e.g. ROSC with return of effective ventilations and/or mentation) may never have needed to undergo advanced airway placement, thus biasing our findings toward a negative association between advanced airway placement and survival. We may also infer that patients with an airway already in place at the time of the initiation of CPR had a greater degree of pre-event morbidity, which may account for their poorer survival.

We found that chest compressions for bradycardia (without pulselessness) were much more prevalent among pediatric patients than adult patients, and that pediatric patients received CPR for bradycardia more often in pediatric hospital EDs than in non-pediatric EDs. However, there was no association between CPR for bradycardia and survival outcomes in the overall cohort. A prior analysis of in-hospital pediatric cardiac arrest data from the NRCPR demonstrated an association between CPR for bradycardia and improved survival to discharge.⁴ Current pediatric resuscitation guidelines recommend that chest compressions be considered in children with heart rates <60 bpm and hypoperfusion; no such recommendation currently exists for adults with bradycardia.⁵ The findings of our current analysis do not support the extrapolation of that recommendation outside the pediatric age range.

4.1. Limitations

The GWTG-R database is a multicenter registry with strict operational definitions and rigorous quality assurance. Nonetheless, the issues of data integrity and validity at the level of individual sites must always be considered as a potential limitation in interpreting data from such analyses. Facilities contributing data to the GWTG-R volunteer as enrolling centers. Most pediatric data in the database is derived from a handful of tertiary centers. While our analytic plan used random effects modeling to control for within-center covariance, the generalizability of the results may be limited.

The GWTG-R database allows retrospective analysis only, and detailed data fields on such phenomena as vital signs, laboratory values, or other physiologic data before or during resuscitation is not available. In particular, aside from the initiation of therapeutic hypothermia, data on other post-resuscitation care is not available from this database, including any data on post-arrest neurologic status. This makes our ability to draw inferences about care in the ED and survival to discharge limited. Pre-event medical comorbidities can be designated on data forms when patients are enrolled; however they are dichotomous entries (present or absent) and it is possible that their relative contribution to outcomes from CPR events is under- or overestimated based on the present structure of the database. Additionally, differences in end of life decision making are elusive from the current database structure; e.g., we are unable to analyze any differences in withdrawal of life sustaining therapy between age strata.

Twelve percent of the pediatric patients in this analysis had available data on ROSC but not on longer term outcomes; presumably many or all of these patients were transferred to tertiary facilities following achievement of ROSC in the ED to which they presented. We excluded these patients from analysis of longer term clinical outcomes; it is not possible to determine whether this amounts to a significant source of bias, although we assume that this should lead to an underestimate of survival to discharge among pediatric patients.

The data in the GWTG-R database does not include any details pertinent to pre-hospital management. Events in the GWTG-R database are determined by abstractionist report as either index or non-index events. In our data set of patients in the ED, 949 (5%) of the overall group of patients were labeled as non-index events. It is not clear from the existing database whether a non-index event for a cardiac arrest patient in the ED should be inferred

to mean that patient arrested during their prehospital management (e.g. out-of-hospital arrest) and arrived to the ED having achieved ROSC and then subsequently arrested again. We excluded patients labeled as non-index events with this potentially confounding influence in mind; however, it is possible that there are patients who had CPR in the pre-hospital phase of their care, and we are unable to account for that in our current analysis.

5. Conclusions

Outcomes from cardiac arrest occurring in the emergency department do not differ significantly between children and adults. Significant differences exist between children and adults with respect to patient, event, and treatment characteristics, but these differences were not independently associated with survival. Future studies should evaluate the impact of age-specific therapies for pre-arrest pathophysiology on outcomes from cardiac arrest in the early phases of in-hospital care in the emergency department.

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Patient <ul style="list-style-type: none"> • Age category • Illness category • Pre-event cardiovascular support • Pre-event respiratory support 	Event <ul style="list-style-type: none"> • Immediate cause • Monitored / witness status • Weekend • Shockable rhythm • Subsequent pVT/VF
Treatment <ul style="list-style-type: none"> • Duration of event • Number of epinephrine boluses • Number of defibrillations • CPR for bradycardia • Time to epinephrine • Time to defibrillation • Invasive airway management (airway in place, airway inserted/attempted during event, no airway inserted/attempted during event) 	Hospital <ul style="list-style-type: none"> • Trauma center certification • Number of ED visits annually • Number of PICU beds

Fig. 1.
List of candidate covariates by category.

GWTG-R variable	Facilities (n)	Adult events (n)	Pediatric events (n)	Study variable
Pediatric	13	9	157	Pediatric (n=13)
Adult	590	15336	380	Non-pediatric (n = 595)
Mixed	5	16	0	

Fig. 2.
Hospital variable.

Fig. 3.
Diagram of Utstein outcomes for all events.

Table 1

Patient and event characteristics by patient group.

Covariate	Pediatric (<i>n</i> = 471)	Adult (<i>n</i> = 15,648)	χ^2
<i>Patient characteristics</i>			
Pre-event CV support	75 (14%)	3885 (24%)	<0.001
Pre-event respiratory support	195 (36%)	5135 (32%)	0.04
Illness category			
Medical (cardiac)	121 (26%)	8641 (55%)	<0.001
Medical (noncardiac)	316 (67%)	6599 (42%)	<0.001
Surgical	12 (3%)	386 (3%)	0.9
Other	22 (5%)	22 (<1%)	<0.001
Pre-existing conditions			
None	93 (20%)	1350 (9%)	<0.001
CNS event	88 (19%)	2372 (15%)	0.04
Arrhythmia	92 (20%)	4584 (29%)	<0.001
Congenital heart disease	22 (5%)	83 (<1%)	<0.001
CHF	15 (3%)	1501 (9%)	<0.001
Diabetes mellitus	7 (1%)	3228 (21%)	<0.001
Hepatic insufficiency	4 (<1%)	564 (4%)	<0.001
Hypotension	103 (22%)	4005 (26%)	0.07
Malignancy	17 (3%)	993 (6%)	0.02
Metabolic/electrolyte abnormality	46 (10%)	2028 (13%)	0.04
MI	1 (<1%)	3102 (20%)	<0.001
Pneumonia	18 (4%)	925 (6%)	0.06
Renal insufficiency	23 (5%)	2687 (17%)	<0.001
Respiratory insufficiency	227 (48%)	5990 (38%)	<0.001
Septicemia	45 (10%)	1080 (7%)	0.03
<i>Event characteristics</i>			
Immediate cause			
Active MI	2 (<1%)	2697 (17%)	<0.001
Pulmonary edema	9 (2%)	421 (3%)	0.38
Pulmonary embolism	0	312 (2%)	<0.001
Acute respiratory insufficiency	267 (57%)	6214 (40%)	<0.001
Arrhythmia	200 (42%)	8287 (53%)	<0.001
Hypotension	153 (32%)	5323 (34%)	0.48
Inadequate natural airway	28 (6%)	390 (2%)	<0.001
Status epilepticus	9 (2%)	98 (<1%)	0.004
Metabolic/electrolyte abnormality	51 (11%)	1767 (11%)	0.38
Toxicologic problem	11 (2%)	290 (2%)	0.67
Monitored	334 (62%)	13,364 (82%)	<0.001
Witnessed	422 (79%)	14,365 (88%)	<0.001
Weekend	165 (36%)	5005 (33%)	0.15

Covariate	Pediatric (n = 471)	Adult (n = 15,648)	χ^2
Shockable rhythm	155 (29%)	5386 (33%)	0.04
CPR for bradycardia	131 (24%)	913 (6%)	<0.001
Subsequent VF/pVT	35 (7%)	2773 (17%)	<0.001

CPR: cardiopulmonary resuscitation; VF/pVT: ventricular fibrillation/pulseless ventricular tachycardia; MI: myocardial infarction; CHF: congestive heart failure.

Table 2

Treatment variables by patient group.

Covariate	Pediatric	Adult	<i>p</i>
Number of defibrillations (median, range)	3 (0–9)	2 (0–15)	0.3
Number of epinephrine doses (median, range)	3 (0–15)	2 (0–9)	<0.001
Duration of event in minutes (median, range)	24 (3–141)	17 (2–110)	<0.001
Time from event to CPR (median, range)	0 (0–7)	0 (0–9)	0.4
Time from VF to defibrillation (median, range)	0 (0–19)	0 (0–10)	0.4
Time from event to epinephrine (median, range)	2 (–32 to 23)	2 (–8 to 23)	0.2
Airway in place at time of event (<i>n</i> , %)	167/537 (31%)	5410/16,237 (33%)	0.3
Airway placement attempted during event (<i>n</i> , %)	345/537 (64%)	8893/16,237 (55%)	<0.001
No airway placement attempted during event (<i>n</i> , %)	25/537 (5%)	1934/16,237 (12%)	<0.001

Table 3

Multivariate analysis.

Covariate	Adjusted OR (95% CI)		
	ROSC	24 h survival	Survival to discharge
<i>Hospital factors</i>			
Trauma center certification	1.36 (1.14–1.61)	1.38 (1.17–1.63)	1.28 (1.06–1.54)
Annual ED visits (compared with >7000)			
• 0–3999	0.71 (0.53–0.95)	0.64 (0.48–0.85)	0.65 (0.48–0.88)
• 4000–6999	0.84 (0.67–1.05)	0.84 (0.69–1.02)	0.89 (0.71–1.12)
<i>Patient factors</i>			
Pediatric patient	1.02 (0.75–1.42)	0.94 (0.64–1.39)	1.27 (0.81–1.98)
Illness category: medical – cardiac	0.80 (0.71–0.90)	1.05 (0.92–1.21)	1.18 (1.02–1.37)
Respiratory support	1.01 (0.88–1.16)	0.97 (0.84–1.12)	0.82 (0.68–0.98)
CV support	0.87 (0.75–1.00)	0.71 (0.61–0.84)	0.79 (0.66–0.94)
Monitored or witnessed patient	1.46 (1.14–1.88)	1.29 (0.96–1.72)	1.61 (1.20–2.17)
Pre-existing conditions			
• CHF this admission	1.53 (1.33–1.77)	1.51 (1.29–1.77)	1.41 (1.17–1.70)
• MI this admission	1.49 (1.32–1.68)	1.39 (1.22–1.59)	1.60 (1.36–1.88)
• Hypotension	1.17 (1.04–1.32)	0.84 (0.73–0.97)	0.63 (0.51–0.76)
• Respiratory insufficiency	1.20 (1.09–1.33)	1.21 (1.08–1.36)	1.22 (1.04–1.40)
<i>Event factors</i>			
Shockable rhythm	1.72 (1.55–1.93)	1.86 (1.67–2.07)	2.29 (2.02–2.59)
Immediate cause: hypotension	0.98 (0.87–1.12)	0.82 (0.71–0.95)	0.83 (0.70–1.00)
<i>Treatment factors</i>			
Advanced airway placement (compared with airway in place)			
• Attempted during event	1.14 (0.99–1.30)	1.40 (1.20–1.64)	1.38 (1.16–1.65)
• Not attempted	1.79 (1.40–2.29)	2.62 (2.04–3.37)	3.83 (2.91–5.06)
Duration of event (per minute)	0.98 (0.97–0.99)	0.98 (0.97–0.99)	0.98 (0.97–0.99)
Epinephrine bolus (per dose)	0.96 (0.94–0.98)	0.96 (0.94–0.97)	0.96 (0.94–0.97)
CPR started for bradycardia	0.87 (0.72–1.05)	0.95 (0.78–1.15)	0.91 (0.69–1.19)