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# Association Between Tracheal Intubation During Pediatric In-Hospital Cardiac Arrest and Survival

**Lars W. Andersen, MD, MPH**, **Tia T. Raymond, MD**, **Robert A. Berg, MD**, **Vinay M. Nadkarni, MD**, **Anne V. Grossestreuer, PhD**, **Tobias Kurth, MD, ScD**, and **Michael W. Donnino, MD**

Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Andersen, Donnino); Department of Anesthesiology, Aarhus University Hospital, Aarhus, Denmark (Andersen); Research Center for Emergency Medicine, Aarhus University Hospital, Aarhus, Denmark (Andersen); Division of Cardiac Critical Care, Department of Pediatrics, Medical City Children's Hospital, Dallas, Texas (Raymond); Department of Anesthesiology and Critical Care, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (Berg, Nadkarni); Department of Pediatrics, University of Pennsylvania Perelman School of Medicine, Philadelphia (Berg, Nadkarni); Department of Anesthesiology and Critical Care, University of Pennsylvania Perelman School of Medicine, Philadelphia (Berg, Nadkarni); Department of Emergency Medicine, University of Pennsylvania, Philadelphia (Grossestreuer); Now with the Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Grossestreuer); Institute of Public Health, Charité–Universitätsmedizin Berlin, Berlin, Germany (Kurth); Department of Medicine, Division of Pulmonary and Critical Care Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Donnino)

**American Heart Association's Get With The Guidelines–Resuscitation Investigators**

**Corresponding Author:** Lars W. Andersen, MD, MPH, Research Center for Emergency Medicine, Aarhus University Hospital, Nørrebrogade 44, Bygning 30, 1. sal, 8000 Aarhus C, Denmark (lwandersen@clin.au.dk).

**Group Information:** The American Heart Association's Get With The Guidelines–Resuscitation (GWTG-R) investigators are listed at the end of this article.

**Author Contributions:** Dr Andersen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Concept and design:* Andersen, Raymond, Berg, Nadkarni, Kurth, Donnino.

*Acquisition, analysis, or interpretation of data:* All Authors.

*Drafting of the manuscript:* Andersen, Nadkarni, Donnino.

*Critical revision of the manuscript for important intellectual content:* All Authors.

*Statistical analysis:* Andersen, Kurth, Grossestreuer.

*Study supervision:* Andersen, Raymond, Berg, Nadkarni, Kurth, Donnino.

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**Get With The Guidelines-Resuscitation (GWTG-R) Investigators:** The Get With The Guidelines-Resuscitation Pediatric Research Task Force includes authors Tia T. Raymond, MD, and Vinay M. Nadkarni, MD, and Alexis A. Topjian, MD, MSCE, Melania Bembea, MD, MPH (Johns Hopkins University School of Medicine); Emilie Allen, MSN, RN, CCRN (Parkland Health & Hospital System); Linda Brown, MD, MSCE (Hasbro Children's Hospital Emergency Medicine); Aaron Calhoun, MD (Pediatric Critical Care —Kosair Children's Hospital); Ericka Fink, MD (University of Pittsburgh School of Medicine); Elizabeth Foglia, MD, MA, and Robert M. Sutton, MD (The Children's Hospital of Philadelphia); Michael G. Gaies, MD, MPH (University of Michigan); Anne-Marie Guerguerian, MD, PhD, and Chris Parshuram, MBChB, DPhil (The Hospital for Sick Children); Punkaj Gupta, MBBS (Arkansas Children's Hospital); Monica Kleinman, MD (Boston Children's Hospital); Lynda J. Knight, MSN, RN, CPN (Stanford Children's Health Hospital); Javier Lasa, MD (Texas Children's Hospital); Peter C. Laussen, MBBS (University of Toronto); and Taylor Sawyer, DO, MEd (Seattle Children's Hospital).

**Derek C. Angus, MD, MPH [Associate Editor]**
*JAMA*, (angusdc@upmc.edu)

## Abstract

**IMPORTANCE—**Tracheal intubation is common during pediatric in-hospital cardiac arrest, although the relationship between intubation during cardiac arrest and outcomes is unknown.

**OBJECTIVE—**To determine if intubation during pediatric in-hospital cardiac arrest is associated with improved outcomes.

**DESIGN, SETTING, AND PARTICIPANTS—**Observational study of data from United States hospitals in the Get With The Guidelines-Resuscitation registry. Pediatric patients (<18 years) with index in-hospital cardiac arrest between January 2000 and December 2014 were included. Patients who were receiving assisted ventilation, had an invasive airway in place, or both at the time chest compressions were initiated were excluded.

**EXPOSURES—**Tracheal intubation during cardiac arrest.

**MAIN OUTCOMES AND MEASURES—**The primary outcome was survival to hospital discharge. Secondary outcomes included return of spontaneous circulation and neurologic outcome. A favorable neurologic outcome was defined as a score of 1 to 2 on the pediatric cerebral performance category score. Patients being intubated at any given minute were matched with patients at risk of being intubated within the same minute (ie, still receiving resuscitation) based on a time-dependent propensity score calculated from multiple patient, event, and hospital characteristics.

**RESULTS—**The study included 2294 patients; 1308 (57%) were male, and all age groups were represented (median age, 7 months [25th-75th percentiles, 21 days, 4years]). Of the 2294 included patients, 1555 (68%) were intubated during the cardiac arrest. In the propensity score-matched cohort (n = 2270), survival was lower in those intubated compared with those not intubated (411/1135 [36%] vs 460/1135 [41%]; risk ratio [RR], 0.89 [95% CI, 0.81–0.99]; $P = .03$). There was no significant difference in return of spontaneous circulation (770/1135 [68%] vs 771/1135 [68%]; RR, 1.00 [95% CI, 0.95–1.06]; $P = .96$) or favorable neurologic outcome (185/987 [19%] vs 211/983 [21%]; RR, 0.87 [95% CI, 0.75–1.02]; $P = .08$) between those intubated and not intubated. The association between intubation and decreased survival was observed in the majority of the sensitivity and subgroup analyses, including when accounting for missing data and in a subgroup of patients with a pulse at the beginning of the event.

**CONCLUSIONS AND RELEVANCE—**Among pediatric patients with in-hospital cardiac arrest, tracheal intubation during cardiac arrest compared with no intubation was associated with decreased survival to hospital discharge. Although the study design does not eliminate the potential for confounding, these findings do not support the current emphasis on early tracheal intubation for pediatric in-hospital cardiac arrest.

Survival rates from pediatric in-hospital cardiac arrest are improving, yet mortality remains high.[1] Most pediatric in-hospital cardiac arrests are precipitated by acute respiratory failure (hypoxia), and relatively few are attributable to primary arrhythmias (eg, ventricular fibrillation or ventricular tachycardia).[2,3] Therefore, the standard paradigm for pediatric in-

hospital cardiopulmonary resuscitation (CPR) focuses on early effective respiratory support to establish adequate oxygenation and ventilation and on high-quality chest compressions to provide adequate myocardial and cerebral blood flow.[4] Although there is increasing evidence supporting the importance of high-quality chest compressions for survival from pediatric in-hospital cardiac arrests,[5] less is known about the importance of invasive airway management during CPR.

Invasive airway management for children is often a challenging and potentially dangerous task. Therefore, it is not surprising that tracheal intubation in the prehospital setting did not improve outcomes compared with bag-valve-mask ventilation during pediatric emergencies, including cardiac arrest.[6] Consequently, recommendations from the International Liaison Committee On Resuscitation Pediatric Task Force and the American Heart Association support the use of bag-valve-mask ventilation as opposed to tracheal intubation in patients with out-of-hospital pediatric cardiac arrest and with a short transport time.[7,8]

In contrast to the prehospital setting, a large proportion of pediatric in-hospital cardiac arrests occur in an intensive care unit, emergency department, or interventional setting (eg, catheterization laboratory or operating room),[9] where the hospital-based personnel are presumably highly trained for invasive airway management and ventilatory support.

The goal of the current investigation was to examine, among pediatric patients with in-hospital cardiac arrest, whether tracheal intubation during cardiac arrest is associated with survival to hospital discharge. Because acute respiratory failure is a common cause of pediatric in-hospital cardiac arrest, it was hypothesized that tracheal intubation during cardiac arrest would be associated with improved survival.

## Methods

### Data Source

Data from the Get With The Guidelines-Resuscitation (GWTG-R) registry were used. This is an American Heart Association-sponsored prospective quality improvement registry of in-hospital cardiac arrests in the United States. The data collection process and reliability have been described in full detail.[10,11] In the registry, cardiac arrest is defined as pulselessness, or a pulse with inadequate perfusion, requiring chest compressions, defibrillation, or both and with a hospital-wide or unit-based emergency response by acute care facility personnel. Hospital-level data (teaching status and type of hospital) were obtained from the American Hospital Association's Annual Survey from 2013.[12]

All participating hospitals in the GWTG-R registry are required to comply with local regulatory guidelines. Because data are used primarily at the local site for quality improvement, sites are granted a waiver of informed consent under the common rule.

### Study Population

The cohort included data submitted to the GWTG-R registry between January 2000 and December 2014. All patients younger than 18 years who had an index cardiac arrest with 1 minute or more of chest compressions were included. Patients were excluded if they were

receiving assisted ventilation, had an invasive airway (including a tracheostomy tube) in place at the time chest compressions were initiated, or both. Furthermore, hospital visitors and cardiac arrests in the delivery room or neonatal intensive care unit were excluded. For the primary analysis and majority of analyses, patients with missing or inconsistent data on tracheal intubation, timing of intubation, timing of the end of resuscitation, timing of pulselessness, survival, or relevant covariates were excluded (537 patients [19%], see Figure 1 for details). These patients were included in a preplanned sensitivity analysis accounting for missing data (see statistical analysis below).

## Intubation and Study Outcomes

Intubation was defined as insertion of a tracheal tube during the cardiac arrest event. Unsuccessful intubation attempts were not counted as intubations. The time to intubation was defined as the time interval in whole minutes from the start of chest compressions until the tracheal tube was inserted. All times in the GWTG-R registry are collected in whole minutes. As such, a time to intubation of 0 minutes indicates that the intubation was performed within the same whole minute as chest compressions were started; a time of 1 minute indicates that intubation was performed within the next whole minute, etc.

The primary outcome was designated a priori as survival to hospital discharge. Secondary outcomes were return of spontaneous circulation (ROSC) and favorable neurologic outcome at hospital discharge. ROSC was defined as no further need for chest compressions (including initiation of cardiopulmonary bypass) that was sustained for longer than 20 minutes. Neurologic outcome was assessed as recommended by the Utstein guidelines[13] using the pediatric cerebral performance category (PCPC) score,[14] where a PCPC score of 1 indicates no neurologic deficit; 2, mild cerebral disability; 3, moderate cerebral disability; 4, severe cerebral disability; 5, coma or vegetative state; and 6, brain death. A PCPC score of 1 and 2 was considered a favorable neurologic outcome, and a PCPC score of 3 to 6 or death was considered a poor neurologic outcome. Prospectively designated sensitivity analyses were performed with different definitions of favorable neurologic outcome: (1) a PCPC score of 1 or 2, or no increase from baseline; (2) a PCPC score of 1,2, or 3; and (3) a PCPC score of 1,2, or 3, or no increase from baseline.[15]

Data abstractors were not blinded to outcomes but were unaware of the hypothesis of the current study.

## Statistical Analyses

The study population was characterized using descriptive statistics. Categorical variables are presented as counts and frequencies and continuous variables as medians with 25th and 75th percentiles. The $\chi^2$ test was used to compare categorical data between independent groups and the Wilcoxon rank sum test to compare continuous variables. The Cochran-Armitage test was used to test for linear trends in tracheal intubation over time.

To assess the adjusted association between tracheal intubation during CPR and survival to hospital discharge, time-dependent propensity score matching was used.[16] A similar methodology has been successfully applied to the adult cardiac arrest population and accounts for the time-dependent nature of interventions during cardiac arrest.[17] If the timing

of intubation is not accounted for, it is likely that the results would be biased toward a harmful effect of intubation, since intubation can be a function of prolonged resuscitation, and prolonged resuscitation is associated with poor outcomes.[18]

The propensity score was calculated using a multivariable Cox proportional hazards model as explained in additional details in the eMethods in the Supplement. All variables presented in Table 1 were included in the propensity score model (see eTable 1 in the Supplement for definitions of preexisting conditions). All variables were chosen a priori based on prior work or clinical reasoning derived from prior publications related to pediatric in-hospital cardiac arrest.[1,11,19,20]

Matching (1:1) on the propensity score was performed using a nearest neighbor-matching algorithm with a maximum caliper of 0.01 of the propensity score. Patients being intubated at any given minute (from minute 0 to minute 15) were separately and sequentially propensity score matched with a patient who was "at risk" of being intubated within the same minute. Patients were matched up until 15 minutes after the cardiac arrest, because intubation at any given minute after 15 minutes was uncommon. At-risk patients included those still undergoing resuscitation (ie, excluding patients with ROSC or resuscitation terminated without ROSC) and who did not receive intubation before or within the same minute. At-risk patients also included patients intubated at a later point, because the matching should not be dependent on future events.[16,17,21,22] For example, a patient intubated at minute 3 was matched with a patient who was at risk of intubation at minute 3 (ie, either a patient intubated after minute 3 or a patient never intubated). Replacement of controls was used to reduce the number of unmatched exposed patients.

To assess the performance of the matching, baseline categorical variables were compared between the matched groups using the Cochran-Mantel-Haenszel test, and standardized differences were calculated for which a difference between −0.1 and 0.1 is generally considered negligible.[23] Using the matched cohort, modified Poisson regression was performed to assess the association between intubation during CPR and survival to hospital discharge obtaining risk ratios (RRs) with robust variance estimates.[24,25] To account for the matching, the correlation between resampled controls, and potential clustering within hospitals, generalized estimating equations were used as described by Miglioretti and Heagerty, accounting for the nonnested nature of these clusters.[26] The results from the regression models are reported as RRs with 95% confidence intervals.

Whether the association between intubation during CPR and survival varied with the duration of the event was examined by adding an interaction term between the intubation variable (yes/no) and time to intubation/matching (ie, time from start of chest compressions to the minute the patient was matched) to the modified Poisson regression model. Time was first treated as a linear continuous variable and next as a categorical variable (0–5, 6–10, and 11–15 minutes).

Three predefined sensitivity analyses were performed. First, multiple imputations were performed to account for missing data. Categorical variables were imputed using the fully conditional specification method, and continuous time variables were imputed using Poisson

distributions as described in more detail in the eMethods in the Supplement. Second, the primary analysis was performed after excluding those patients who received cardiopulmonary bypass (extracorporeal membrane oxygenation) during the event. Third, the main analysis was performed including only those patients who had 2 minutes or more of chest compressions and not including patients intubated 2 minutes or less after the start of chest compressions. A post hoc sensitivity analysis assessing the potential influence of an unmeasured confounder was performed using the method as described by Lin et al.[27] Additional details are provided in the eMethods in the Supplement. As a second post hoc sensitivity analysis, we conducted a traditional propensity score-matched analysis (ie, not accounting for the timing of intubation). Additional details are provided in the eMethods in the Supplement.

As a predefined subgroup analysis, the cohort was restricted to those patients who lost pulse at any time during the event. For this analysis, the time to intubation was calculated as the time from loss of pulse to intubation, and patients who were intubated before pulselessness were excluded. Then an approach similar to that described above was used to assess whether intubation during CPR was associated with outcomes in this subgroup of patients. As a post hoc analysis, a subgroup analysis was also conducted in only those who received CPR for bradycardia and inadequate perfusion (ie, pulse present at initiation of CPR).

Exploratory analyses tested whether the association between intubation during CPR and survival to hospital discharge differed according to multiple subgroups. The subgroups included age group, illness category, whether the patients had preceding respiratory insufficiency, and the location of the event. This was tested by adding interactions between the intubation variable and the subgroup variable of interest to the modified Poisson regression model in the propensity-matched cohort. Given the exploratory nature of these analyses, a more stringent 2-sided $P$ value (<.01) was considered significant.

All hypothesis tests were 2-sided, with a significance level of $P < .05$ apart from the exploratory analyses of subgroup associations. All secondary analyses should be considered exploratory, as no adjustments except as noted were made for multiple comparisons. No power calculation was performed before the study. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc).

## Results

### Characteristics of the Patient Population

The study included 2294 patients (Figure 1); 1308 (57%) were male, and all age groups were represented (median age, 7 months [25th-75th percentiles, 21 days, 4 years]). Of these, 1555 (68%) were intubated during the cardiac arrest. For these patients, the median documented time to successful tracheal intubation from start of compressions was 5 minutes (25th-75th percentiles, 2–11), see Figure 2. There was a decrease in the proportion of patients being intubated over time (79% in 2000 to 62% in 2014, $P = .001$ for linear trend). Only 13 of those intubated (0.8%) received a tracheostomy tube. Baseline characteristics according to intubation status are presented in Table 1.

### Overall Outcomes and Unadjusted Analyses

Overall, 1162 patients (51%) survived to hospital discharge. In unadjusted analysis, tracheal intubation during CPR was associated with decreased survival to hospital discharge (667/1555 [43%] vs 495/739 [67%]; RR, 0.64 [95% CI, 0.59-0.69]; $P < .001$). ROSC was achieved in 1766 patients (77%). In unadjusted analysis, tracheal intubation during CPR was associated with decreased ROSC (1130/1555 [73%] vs 636/739 [86%]; RR, 0.84 [95% CI, 0.81–0.88]; $P < .001$). Data on neurologic outcomes at hospital discharge was missing for 414 patients (18%), all of whom survived, since nonsurvivors were classified as poor neurologic outcome. In patients with data on neurologic outcome, 557 of 1880 (30%) had a favorable neurologic outcome, which corresponds to 557 of 748 survivors (74%). In unadjusted analysis, tracheal intubation during CPR was associated with decreased favorable neurologic outcome (313/1318 [24%] vs 244/562 [43%]; RR, 0.55 [95% CI, 0.48–0.63]; $P < .001$).

### Time-Dependent Propensity-Matched Multivariable Analyses

Of the 2294 patients, 2270 were matched based on the propensity score. The baseline characteristics of the matched cohort are presented in Table 2. The groups were well matched on all included variables (all $P$ values >.10 and standardized differences between −0.1 and 0.1). In the propensity score-matched cohort, survival to hospital discharge was lower in those intubated compared with those not intubated during CPR (411/1135 [36%] vs 460/1135 [41%]; RR, 0.89 [95% CI, 0.81–0.99]; $P = .03$). There was no significant difference in ROSC (770/1135 [68%] vs 771/1135 [68%]; RR, 1.00 [95% CI, 0.95–1.06]; $P = .96$) or favorable neurologic outcome (185/987 [19%] vs 211/983 [21%]; RR, 0.87 [95% CI, 0.75–1.02]; $P = .08$) between those intubated and not intubated during CPR. The results are summarized in Figure 3. The results were similar in magnitude with each of the different sensitivity definitions of favorable neurologic outcome (eTable 2 in the Supplement). None of the interactions as described in the methods sections were significant, indicating no significant subgroup difference in this study for age group, illness category, preceding respiratory insufficiency, or the location of the event.

### Timing of Intubation

There was no significant interaction between tracheal intubation during CPR and the timing of the matching for any of the outcomes for either the linear ($P = .50$) or the categorical ($P = .86$) version of time. Thus, the association between tracheal intubation during CPR and survival did not change with the duration of the cardiac arrest.

### Sensitivity Analyses

The sensitivity analysis accounting for missing data included 2831 patients. Between 2736 and 2768 patients were matched in the 10 imputed data sets. The combined estimate from the 10 data sets showed that tracheal intubation during CPR was associated with decreased survival (RR, 0.88 [95% CI, 0.79–0.99]; $P = .03$) and decreased favorable neurologic outcome (RR, 0.85 [95% CI, 0.73–0.98]; $P = .03$). There was no association with ROSC (RR, 0.99 [95% CI, 0.93–1.05]; $P = .79$).

One hundred eleven patients (5%) received cardiopulmonary bypass (ie, extracorporeal CPR) during the event, 2 patients had missing data on this variable, and 2181 patients were included in the analysis excluding those patients; 2116 patients were matched based on the propensity score. In this cohort, tracheal intubation during CPR was associated with decreased survival (RR, 0.90 [95% CI, 0.81–0.99]; *P* = .04). Tracheal intubation during CPR was not associated with ROSC (RR, 1.01 [95% CI, 0.95–1.08]; *P* = .73) and not associated with favorable neurologic outcome (RR, 0.95 [95% CI, 0.82–1.09]; *P* = .44). Survival to hospital discharge was 41% (46/111) in those who received cardiopulmonary bypass, and 87% (97/111) were intubated during CPR.

In the sensitivity analysis only including patients receiving at least 2 minutes of chest compression, 1762 were propensity-score matched. In this group, tracheal intubation during CPR was associated with decreased survival to hospital discharge (RR, 0.90 [95% CI, 0.80–1.00]; *P* = .04). Intubation was not associated with ROSC (RR, 1.00 [95% CI, 0.94–1.07]; *P* = .91) or favorable neurologic outcomes (RR, 0.89 [95% CI, 0.73–1.10]; *P* = .29).

The results for the post hoc sensitivity analysis exploring the potential influence of an unmeasured confounder are presented in the eFigure in the Supplement. Based on the findings of this analysis, it is unlikely that an unmeasured confounder is masking a positive association (ie, that intubation is associated with improved survival). For example, for the point estimate of the adjusted RR to be 1.20 (ie, a clinically meaningful effect), the unmeasured binary confounder would have to be prevalent and strongly associated with intubation (eg, a prevalence of 20% in those not intubated and 40% in those intubated) and be very strongly associated with increased mortality (an RR between 3.5 and 4.0), independent of measured confounders. None of the measured confounders (Table 1) comes close to fulfilling these criteria.

For the post hoc analysis using traditional propensity score matching, 1388 patients were matched. In this analysis, intubation compared with no intubation was associated with decreased survival (368/694 [53%] vs 458/694 [66%]; RR, 0.80 [95% CI, 0.71–0.91]; *P* < .001), decreased ROSC (555/694 [80%] vs 591/694 [85%]; RR, 0.94 [95% CI, 0.88–1.00]; *P* = .05), and decreased good neurologic outcome (193/573 [34%] vs 231/536 [43%]; RR, 0.78 [95% CI, 0.66–0.93]; *P* = .005).

### Subgroup Analyses

In the subgroup of patients documented as pulseless (ie, excluding those with severe bradycardia requiring CPR), 1494 patients were included. Of these patients, 1019 (68%) were intubated during CPR, and overall survival to hospital discharge was 40%. The median time from pulselessness to successful intubation in these patients was 5 minutes (25th-75th percentiles, 2–10). For the subgroup analyses, 1706 patients were matched; the groups were well matched on all included variables after propensity score matching (all *P* values >.10 and standardized differences between −0.1 and 0.1; see eTable 3 in the Supplement). In this subgroup, tracheal intubation during CPR was not associated with survival to hospital discharge (RR, 0.88 [95% CI, 0.77–1.01]; *P* = .07). Intubation also was not associated with ROSC (RR, 0.98 [95% CI, 0.91–1.05]; *P* = .53) or favorable neurologic outcomes (RR, 0.83 [95% CI, 0.68–1.02]; *P* = .07).

The post hoc analysis of the subgroup of patients who started the event with a pulse (ie, severe bradycardia requiring CPR) included 935 patients, with an overall survival to hospital discharge of 66%. Of these, 223 (24%) lost their pulse during the event. Five hundred seventy-three patients (61%) were intubated, with a median time from start of chest compressions to intubation of 6 minutes (25th-75th percentiles, 2–11). Six hundred fifty patients were matched. The groups were reasonably well matched on all included variables after propensity score matching (all $P$ values >.01 and standardized differences between −0.18 and 0.18; see eTable 4 in the Supplement). In this subgroup, tracheal intubation during CPR was associated with decreased survival to hospital discharge (RR, 0.86 [95% CI, 0.75–0.98]; $P = .03$) and decreased favorable neurologic outcome (RR, 0.72 [95% CI, 0.58–0.90]; $P = .003$). Intubation was not associated with ROSC (RR, 1.00 [95% CI, 0.95–1.06]; $P = .90$).

## Discussion

Although tracheal intubation to achieve effective oxygenation and ventilation is a basic tenet of advanced CPR for pediatric in-hospital cardiac arrests, this study was unable to demonstrate any association of improvement in survival with tracheal intubation during CPR when using time-dependent propensity score matching in this large multicenter study of pediatric in-hospital cardiac arrest. Importantly, this study found that tracheal intubation during CPR was associated with decreased survival to hospital discharge in the primary propensity-matched analysis. This association was consistently demonstrable with several sensitivity and subgroup analyses.

Tracheal intubation is the current standard of care in the setting of in-hospital cardiac arrest and is commonly prioritized and accomplished during in-hospital pediatric cardiac arrest. The data confirmed that this is the most common approach, as 68% of children who were not already intubated or receiving assisted ventilation at the time of CPR were intubated during CPR. Although recent guidelines have deemphasized the focus on tracheal intubation during cardiac arrest, especially in the adult population, the optimal approach to airway management during cardiac arrest in general and particularly pediatric in-hospital cardiac arrest remains unknown.[7,28] Underlying pulmonary or airway disease and a presumed respiratory etiology are common in pediatric in-hospital cardiac arrest,[2,3,29] providing the rationale for invasive airway management. However, tracheal intubation during CPR also carries potential complications and risk of adverse events.[30] Intubation may result in interruptions of chest compressions[31] or in delay of other interventions such as defibrillation, achieving vascular access, or epinephrine administration, which could influence outcomes.[15,32] In addition, the resuscitation leader may also be the most skilled operator, so the choice to intubate during CPR may prevent the resuscitation leader from attending to non-airway-related resuscitation efforts. Another potential detrimental effect of tracheal intubation is hyperventilation and increased intrathoracic pressure, which has been found to be common in cardiac arrest and can result in worse outcomes in animal models.[33–35] Importantly, a malpositioned tracheal tube could result in poor oxygenation and ventilation, particularly if not recognized rapidly.

Existing literature on tracheal intubation during pediatric in-hospital cardiac arrest is scarce.[36] Gupta et al[36] conducted a retrospective review of pediatric intensive care unit cardiac arrests at a single center. Of 391 patients, 194 (50%) were not intubated or receiving invasive mechanical ventilation prior to the arrest. In this subgroup, the authors found no association between the timing of invasive airway placement (tracheal intubation) and survival or favorable neurologic outcome, but the power of their study to find a difference was limited. Their findings are consistent with those reported for adult in-hospital cardiac arrests[37] and consistent with those reported here. However, the analytic methodologies, multicenter data, and size of the database differ substantially. In the current analysis, the association between the timing of intubation during CPR and outcomes was assessed by adding an interaction term between intubation and the timing of intubation and matching to the model. This interaction was nonsignificant, indicating that the association between intubation during CPR and outcomes did not change with the duration of the arrest.

In the out-of-hospital setting, a quasi-randomized trial including 591 children in cardiac arrest found no difference in outcomes between patients in cardiac arrest receiving intubation compared with bag-valve-mask ventilation (24/301 vs 24/290 survivors).[6] In a large observational study of out-of-hospital cardiac arrest in adults, Hasegawa et al[38] found that tracheal intubation as compared with bag-valve-mask ventilation was associated with decreased odds of survival and decreased favorable neurologic outcome. Given the substantial differences between in-hospital and out-of-hospital cardiac arrest[3] and between pediatric and adult cardiac arrest,[11] any direct comparison to the current study is challenging.

In this study of in-hospital pediatric cardiac arrest, time-dependent propensity score matching was used, which allows for adjustment for covariates, including time-dependent covariates, and adjustment for the time-dependent risk of being intubated during CPR–something not possible using traditional regression.[16,21] As described in detail in the Methods section, this approach is superior to traditional regression or propensity score matching in situations in which a time-dependent intervention is assessed. Furthermore, the practical relevance of using this approach has previously been shown in relation to 2 high-impact observational studies regarding epinephrine administration in out-of-hospital cardiac arrest. The 2 studies used the same out-of-hospital database, but one used time-dependent propensity score matching,[17] whereas the other used traditional propensity score matching,[39] ultimately yielding differing results. One potential reason for these inconsistent results is that an intracardiac arrest intervention (eg, epinephrine or intubation) can be a function of the duration of the cardiac arrest (ie, patients are more likely to receive the intervention if the cardiac arrest is prolonged), thereby confounding the results. Moreover, the intervention might influence the duration of the event (ie, a patient being intubated might have ROSC because of the intubation), and adjusting for duration of the arrest is therefore difficult when using traditional propensity score matching or regression. The use of time-dependent propensity matching addresses these issues and allows for slightly different interpretation of the results. Specifically, the effect estimates (risk ratios) should be interpreted as the risk of the outcome in those being intubated during CPR at a given minute (from 0 to 15) relative to the risk of the outcome in those not being intubated during CPR at that given minute, which include those being intubated at later time points. This interpretation is more clinically

relevant, because a clinician might consider intubating a patient at any given minute with future events being unknown.

The result of the analysis using traditional propensity score matching indicated a stronger association between intubation and poor outcome. However, as discussed above, this analysis should be interpreted with caution, as it did not take into account the timing of intubation.

Although an association between intubation and decreased survival to hospital discharge was found, no significant association between intubation and neurologic outcome was seen in the main time-dependent propensity-matched multivariable analysis. There are a number of possible explanations for this finding. First, the current data set had a relatively high frequency of missing data on neurologic outcome (18%, corresponding to 36% of survivors), which limits the power and interpretability of the findings. Second, neurologic outcome was based on a nongranular scoring system,[40] for which there might be significant variability in reporting, biasing the results toward the null hypothesis. These potential explanations are supported by the findings of similar point estimates for the risk ratios for survival and favorable neurologic outcome but wider confidence intervals for the latter, resulting in nonsignificant findings. These concerns prompted this study, a priori, to use survival–an objective and almost uniformly reported outcome–as the primary outcome measurement.

The results of the current study should be interpreted in the context of the study design and several limitations. First, this was an observational study, and unmeasured confounders could have influenced the results. The registry does not have data on the specific indication for intubation, data on clinician experience or background, quantitative data on the quality of cardiopulmonary resuscitation, or data on the effectiveness of noninvasive oxygenation and ventilation prior to intubation during CPR. However, the sensitivity analysis assessing the potential influence of an unmeasured confounder indicated that any unmeasured confounder would be unlikely to mask a positive association between intubation and survival. The lack of data on clinician experience and background also limits the ability to assess whether intubation could be beneficial if provided by more experienced clinicians and the ability to adjust for clustering by clinician. Second, intubation attempts are not recorded in the registry, and unsuccessful intubation attempts are classified as “not intubated” and were therefore included in that group in the analyses. This is in contrast to the intent-to-treat principle most often used in randomized clinical trials and could have biased the results, especially if failed intubation attempts during CPR led to poor outcomes. However, this likely would have biased the results toward the null. Third, the GWTG-R registry has very limited information on post-ROSC care, and we were therefore unable to describe this aspect. Fourth, the study may have been underpowered to detect some clinically relevant associations, especially for neurologic outcomes and interactions.

## Conclusions

Among pediatric patients with in-hospital cardiac arrest, tracheal intubation during cardiac arrest compared with no intubation was associated with decreased survival to hospital discharge. Although the study design does not eliminate the potential for confounding, these

findings do not support the current emphasis on early tracheal intubation for pediatric in-hospital cardiac arrest.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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## Key Points

**Question**

Is tracheal intubation during pediatric in-hospital cardiac arrest associated with a difference in survival?

**Findings**

In this observational study including 2270 matched patients, tracheal intubation during pediatric cardiac arrest was significantly associated with decreased survival to hospital discharge (36% for those intubated compared with 41% for those not intubated).

**Meaning**

Although the study design does not eliminate the potential for confounding, these findings do not support the current emphasis on early tracheal intubation for pediatric in-hospital cardiac arrest.

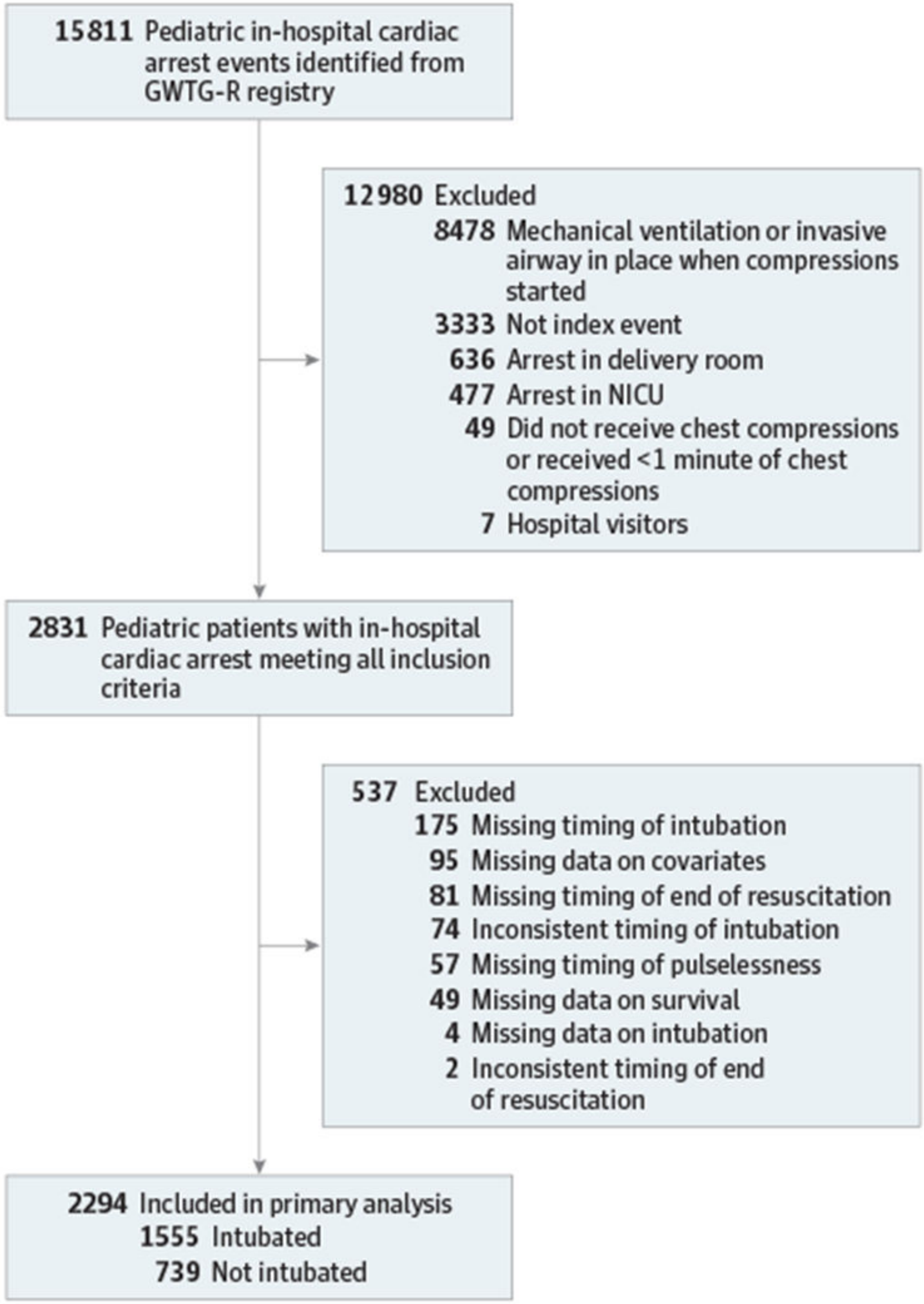


**Figure 1.**

Patient Selection for Study of Tracheal Intubation During Pediatric Cardiac Arrest

GWTG-R, Get With The Guidelines-Resuscitation; IHCA indicates in-hospital cardiac arrest; NICU, neonatal intensive care unit.

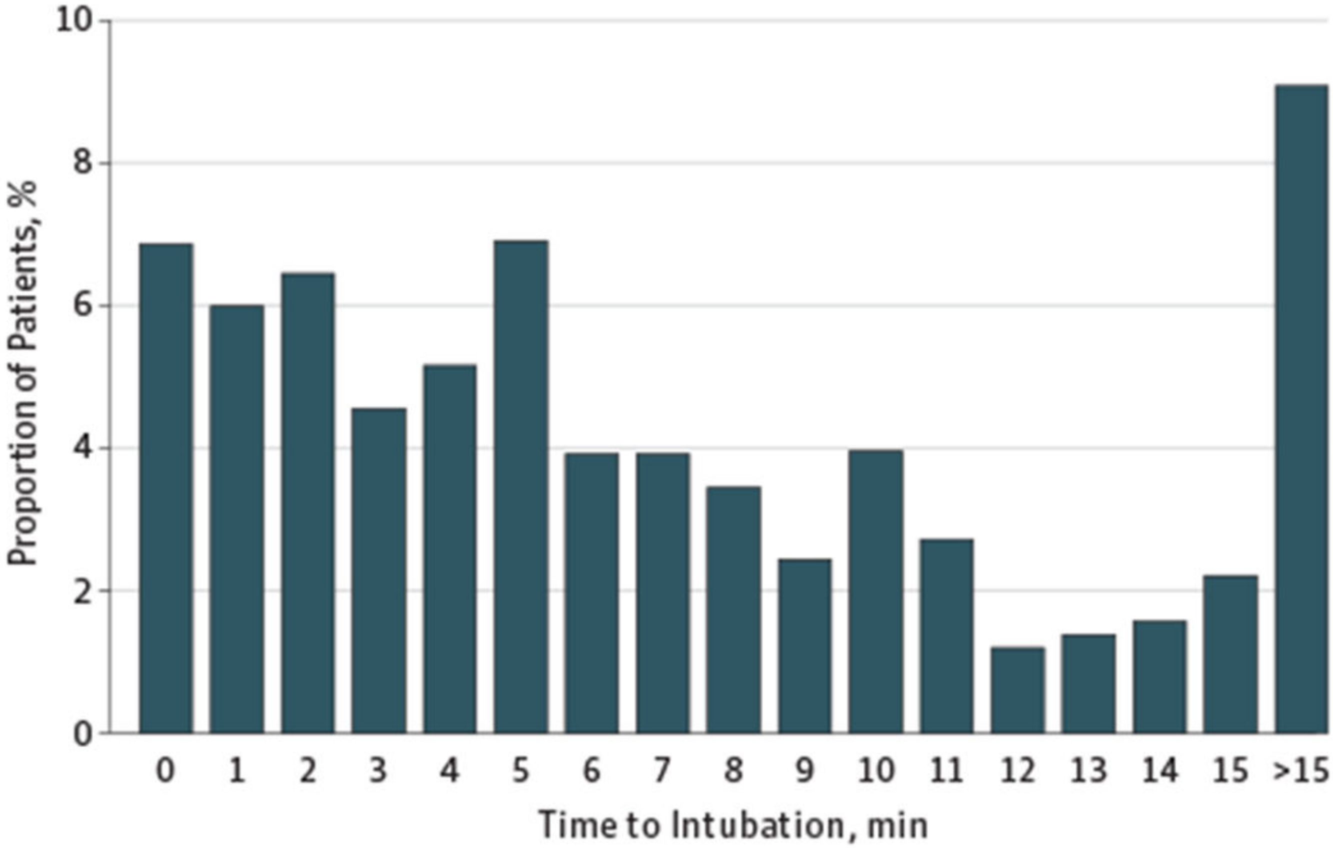


**Figure 2.**

Distribution of Time to Intubation

Distribution of time from start of chest compression to documented successful intubation during cardiopulmonary resuscitation (CPR) in those intubated. Of the 1555 patients (68%) intubated during the CPR event, the median time to intubation from start of chest compressions was 5 minutes (25th-75th percentiles, 2–11). Data on time to intubation were recorded in whole minutes. Time to intubation of 0 minutes indicates that intubation was performed in the same whole minute as the start of chest compressions.

| | Not Intubated | Intubated | |
|---|---|---|---|
| | Patients With Events, No./Total (%) | Patients With Events, No./Total (%) | Risk Ratio (95% CI) |
| **Survival** | | | |
| Unadjusted analysis | 495/739 (67) | 667/1555 (43) | 0.64 (0.59-0.69) |
| Main adjusted analysis | 460/1135 (41) | 411/1135 (36) | 0.89 (0.81-0.99) |
| Sensitivity analyses | | | |
| Imputation of missing data | 580/1376 (42) | 513/1376 (37) | 0.88 (0.79-0.99) |
| Excluding patients who received CPB | 426/1058 (40) | 382/1058 (36) | 0.90 (0.81-0.99) |
| Excluding patients who received <2 min of chest compressions | 343/881 (39) | 307/881 (35) | 0.90 (0.80-1.00) |
| Subgroup analyses | | | |
| Patients who were pulseless at any time | 288/853 (34) | 254/853 (30) | 0.88 (0.77-1.01) |
| Patients with pulse present at initiation of CPR | 193/325 (59) | 166/325 (51) | 0.86 (0.75-0.98) |
| **ROSC** | | | |
| Unadjusted analysis | 636/739 (86) | 1130/1555 (73) | 0.84 (0.81-0.88) |
| Main adjusted analysis | 771/1135 (68) | 770/1135 (68) | 1.00 (0.95-1.06) |
| Sensitivity analyses | | | |
| Imputation of missing data | 952/1376 (69) | 944/1376 (69) | 0.99 (0.93-1.05) |
| Excluding patients who received CPB | 690/1058 (65) | 698/1058 (66) | 1.01 (0.95-1.08) |
| Excluding patients who received <2 min of chest compressions | 590/881 (67) | 592/881 (67) | 1.00 (0.94-1.07) |
| Subgroup analyses | | | |
| Patients who were pulseless at any time | 530/853 (62) | 518/853 (61) | 0.98 (0.91-1.05) |
| Patients with pulse present at initiation of CPR | 281/325 (86) | 282/325 (87) | 1.00 (0.95-1.06) |
| **Favorable neurologic outcome** | | | |
| Unadjusted analysis | 244/563 (43) | 313/1318 (24) | 0.55 (0.48-0.63) |
| Main adjusted analysis | 211/983 (21) | 185/987 (19) | 0.87 (0.75-1.02) |
| Sensitivity analyses | | | |
| Imputation of missing data | 351/1376 (26) | 298/1376 (22) | 0.85 (0.73-0.98) |
| Excluding patients who received CPB | 178/899 (20) | 173/923 (19) | 0.95 (0.82-1.09) |
| Excluding patients who received <2 min of chest compressions | 154/762 (20) | 139/769 (18) | 0.89 (0.73-1.10) |
| Subgroup analyses | | | |
| Patients who were pulseless at any time | 132/758 (17) | 111/768 (14) | 0.83 (0.68-1.02) |
| Patients with pulse present at initiation of CPR | 107/254 (42) | 79/260 (30) | 0.72 (0.58-0.90) |

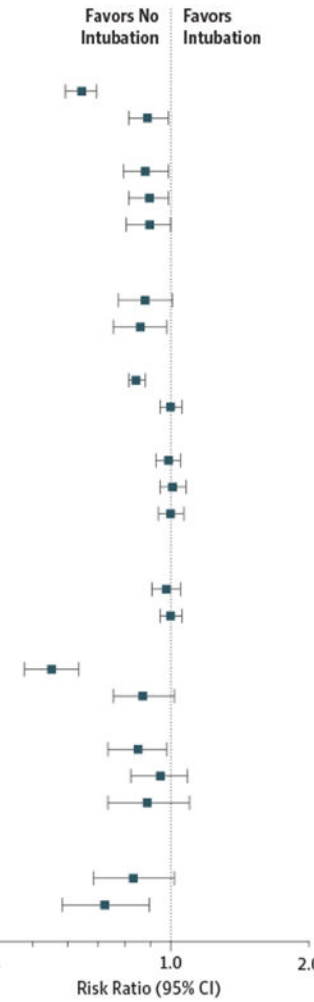


**Figure 3.**

Main and Sensitivity or Secondary Analyses According to Outcome

Unadjusted and adjusted analyses as well as sensitivity analyses and the subgroups of pulseless patients and patients with a pulse at the beginning of the event for the primary outcome survival to hospital discharge and the secondary outcomes return of spontaneous circulation (ROSC) and favorable neurologic outcome at hospital discharge. ROSC was defined as no further need for chest compressions that was sustained for greater than 20 minutes. Neurologic outcome was determined using the pediatric cerebral performance category (PCPC) score, for which a PCPC score of 1 indicates no neurologic deficit; 2, mild cerebral disability; 3, moderate cerebral disability; 4, severe cerebral disability; 5, coma or vegetative state; and 6, brain death. A PCPC score of 1 and 2 was considered a favorable neurologic outcome, and a PCPC score of 3 to 6 or death was considered a poor neurologic outcome. The “main adjusted” analysis refers to the multivariable time-dependent propensity

score-matched analysis. CPB indicates cardiopulmonary bypass; CPR, cardiopulmonary resuscitation.

**Table 1.**

Characteristics of the Study Population

| | No. (%) | | |
|---|---|---|---|
| **Characteristic** | **No Intubation (n = 739)** | **Intubation (n = 1555)** | ***P* Value** |
| Demographics | | | |
| Sex | | | |
| Female | 328 (44) | 658 (42) | .35 |
| Male | 411 (56) | 897 (58) | |
| Age group | | | |
| Neonate (<1 mo) | 194 (26) | 414 (27) | .50 |
| Infant (1 mo to <1 y) | 226 (31) | 434 (28) | |
| Child (1 y to 12 y) | 226 (31) | 485 (31) | |
| Adolescent (>12 y) | 93 (13) | 222 (14) | |
| Illness category | | | |
| Medical | | | <.001 |
| Cardiac | 155 (21) | 301 (19) | |
| Noncardiac | 326 (44) | 690 (44) | |
| Surgical | | | |
| Cardiac | 98 (13) | 258 (17) | |
| Noncardiac | 111 (15) | 157 (10) | |
| Newborn[a] | 49 (7) | 149 (10) | |
| Preexisting conditions[b] | | | |
| Heart failure prior to this admission | 53 (7) | 138 (9) | .17 |
| Heart failure this admission | 59 (8) | 151 (10) | .18 |
| Hypotension | 123 (17) | 246 (16) | .62 |
| Respiratory insufficiency | 326 (44) | 685 (44) | .98 |
| Hepatic insufficiency | 23 (3) | 45 (3) | .77 |
| Renal insufficiency | 45 (6) | 125 (8) | .10 |
| Metabolic or electrolyte abnormality | 70 (9) | 165 (11) | .40 |
| Acute nonstroke CNS event | 36 (5) | 70 (5) | .69 |
| Baseline depression in CNS function | 102 (14) | 215 (14) | .99 |
| Metastatic or hematologic malignancy | 27 (4) | 75 (5) | .20 |
| Pneumonia | 48 (7) | 107 (7) | .73 |
| Septicemia | 63 (9) | 158 (10) | .21 |
| **Location and Time of Arrest** | | | |
| Location | | | |
| Emergency department | 99 (13) | 328 (21) | <.001 |
| Intensive care unit | 363 (49) | 657 (42) | |
| Floor | | | |

| Characteristic | No. (%) | | P Value |
|---|---|---|---|
| | No Intubation (n = 739) | Intubation (n = 1555) | |
| Without telemetry | 122 (17) | 261 (17) | |
| With telemetry/step-down unit | 39 (5) | 79 (5) | |
| Other[c] | 116 (16) | 230 (15) | |
| Time of week | | | |
| Weekend[d] | 206 (28) | 469 (30) | .26 |
| Weekday | 533 (72) | 1086 (70) | |
| Time of day | | | |
| Nighttime[e] | 226 (31) | 436 (28) | .21 |
| Daytime | 513 (69) | 1119 (72) | |
| Year of arrest | | | |
| 2000–2002 | 46 (6) | 150 (10) | .005 |
| 2003–2004 | 72 (10) | 203 (13) | |
| 2005–2006 | 129 (17) | 229 (15) | |
| 2007–2008 | 110 (15) | 247 (16) | |
| 2009–2010 | 122 (17) | 257 (17) | |
| 2011–2012 | 135 (18) | 253 (16) | |
| 2013–2014 | 125 (17) | 216 (14) | |
| Arrest Characteristics | | | |
| Witnessed | | | |
| Yes | 664 (90) | 1349 (87) | .03 |
| No | 75 (10) | 206 (13) | |
| Monitored | | | |
| Yes | 606 (82) | 1128 (73) | <.001 |
| No | 133 (18) | 427 (27) | |
| Pulseless | | | |
| At the beginning of the event | 377 (51) | 982 (63) | <.001 |
| During the event | 41 (6) | 182 (12) | |
| Never | 321 (43) | 391 (25) | |
| Initial pulseless rhythm[f] | | | |
| Nonshockable | 278 (67) | 876 (75) | <.001 |
| Shockable | 61 (15) | 106 (9) | |
| Unknown | 79 (19) | 182 (16) | |
| **Hospital Characteristics** | | | |
| Type of hospital | | | |
| Primarily children | 317 (43) | 607 (39) | .08 |
| Primarily adult | 422 (57) | 948 (61) | |
| Teaching status | | | |

| Characteristic | No. (%) | | P Value |
|---|---|---|---|
| | No Intubation (n = 739) | Intubation (n = 1555) | |
| Major | 518 (70) | 933 (60) | <.001 |
| Minor | 157 (21) | 424 (27) | |
| Nonteaching | 64 (9) | 198 (13) | |

Abbreviation: CNS, central nervous system.

[a]Defined as being born on the current admission.

[b]See eTable 1 in the Supplement for definitions.

[c]Including ambulatory or outpatient clinics, diagnostic or interventional areas, operating room, postanesthesia recovery room, rehabilitation units, same-day surgical areas, and "other."

[d]Friday 11 PM to Monday 7 AM.

[e]11:00 PM to 6:59 AM.

[f]Only including those patients who lost pulse at any time (n = 418 not intubated and n = 1164 intubated).

**Table 2.**

Characteristics of the Study Population in the Matched Cohort

| Characteristic | No. (%) No Intubation (n = 1135) | No. (%) Intubation (n = 1135) | *P* Value | Standardized Difference |
|---|---|---|---|---|
| Demographics | | | | |
| Sex | | | | |
| Female | 498 (44) | 481 (42) | .46 | −0.030 |
| Male | 637 (56) | 654 (58) | | 0.030 |
| Age group | | | | |
| Neonate (<1 mo) | 308 (27) | 290 (26) | .53 | −0.036 |
| Infant (1 mo to <1 y) | 294 (26) | 302 (27) | | 0.016 |
| Child (1 y to 12 y) | 355 (31) | 364 (32) | | 0.017 |
| Adolescent (>12 y) | 178 (16) | 179 (16) | | 0.002 |
| Illness category | | | | |
| Medical | | | .66 | |
| Cardiac | 228 (20) | 230 (20) | | 0.004 |
| Noncardiac | 505 (44) | 495 (44) | | −0.018 |
| Surgical | | | | |
| Cardiac | 176 (16) | 198 (17) | | 0.052 |
| Noncardiac | 114 (10) | 113 (10) | | −0.003 |
| Newborn[a] | 112 (10) | 99 (9) | | −0.040 |
| Preexisting conditions[b] | | | | |
| Heart failure prior to this admission | 101 (9) | 111 (10) | .47 | 0.029 |
| Heart failure this admission | 108 (10) | 118 (10) | .47 | 0.030 |
| Hypotension | 188 (17) | 187 (16) | .95 | −0.002 |
| Respiratory insufficiency | 507 (45) | 476 (42) | .18 | −0.055 |
| Hepatic insufficiency | 36 (3) | 34 (3) | .81 | −0.010 |
| Renal insufficiency | 73 (6) | 97 (9) | .06 | −0.020 |
| Metabolic or electrolyte abnormality | 132 (12) | 125 (11) | .65 | −0.020 |
| Acute nonstroke CNS event | 44 (4) | 48 (4) | .68 | 0.018 |
| Baseline depression in CNS function | 176 (16) | 165 (15) | .51 | −0.027 |
| Metastatic or hematologic malignancy | 65 (6) | 62 (5) | .78 | −0.012 |
| Pneumonia | 75 (7) | 78 (7) | .80 | 0.011 |
| Septicemia | 119 (10) | 118 (10) | .94 | −0.003 |
| **Location and Time of Arrest** | | | | |
| Location | | | | |
| Emergency department | 265 (23) | 256 (23) | .37 | −0.019 |
| Intensive care unit | 468 (41) | 469 (41) | | 0.002 |
| Floor | | | | |

| Characteristic | No. (%) | | *P* Value | Standardized Difference |
|---|---|---|---|---|
| | No Intubation (n = 1135) | Intubation (n = 1135) | | |
| Without telemetry | 187 (16) | 187 (16) | | 0.000 |
| With telemetry/step-down unit | 65 (6) | 57 (5) | | −0.031 |
| Other[c] | 150 (13) | 166 (15) | | 0.041 |
| Time of week | | | | |
| Weekend[d] | 351 (31) | 332 (29) | .38 | −0.037 |
| Weekday | 784 (69) | 803 (71) | | 0.037 |
| Time of day | | | | |
| Nighttime[e] | 315 (28) | 310 (27) | .80 | −0.010 |
| Daytime | 820 (72) | 825 (73) | | 0.010 |
| Year of arrest | | | | |
| 2000–2002 | 97 (9) | 123 (11) | .20 | 0.078 |
| 2003–2004 | 161 (14) | 163 (14) | | 0.005 |
| 2005–2006 | 174 (15) | 179 (16) | | 0.012 |
| 2007–2008 | 178 (16) | 177 (16) | | −0.002 |
| 2009–2010 | 207 (18) | 177 (16) | | −0.071 |
| 2011–2012 | 180 (16) | 168 (15) | | −0.029 |
| 2013–2014 | 138 (12) | 148 (13) | | 0.027 |
| Arrest Characteristics | | | | |
| Witnessed | | | | |
| Yes | 972 (86) | 975 (86) | .85 | 0.008 |
| No | 163 (14) | 160 (14) | | −0.008 |
| Monitored | | | | |
| Yes | 805 (71) | 807 (71) | .92 | 0.004 |
| No | 330 (290) | 328 (29) | | −0.004 |
| Pulseless | | | | |
| At the beginning of the event | 788 (69) | 774 (68) | .64 | −0.027 |
| During the event | 135 (12) | 134 (12) | | −0.003 |
| Never | 212 (19) | 227 (20) | | 0.034 |
| Initial pulseless rhythm[f] | | | | |
| Nonshockable | 699 (76) | 693 (76) | .89 | 0.014 |
| Shockable | 84 (9) | 88 (10) | | 0.020 |
| Unknown | 140 (15) | 127 (14) | | −0.034 |
| Hospital Characteristics | | | | |
| Type of hospital | | | | |
| Primarily children | 447 (39) | 420 (37) | .20 | −0.049 |
| Primarily adult | 688 (61) | 715 (63) | | 0.049 |
| Teaching status | | | | |

| Characteristic | No. (%) | | P Value | Standardized Difference |
|---|---|---|---|---|
| | No Intubation (n = 1135) | Intubation (n = 1135) | | |
| Major | 679 (60) | 658 (58) | .52 | −0.038 |
| Minor | 302 (27) | 322 (28) | | 0.040 |
| Nonteaching | 154 (14) | 155 (14) | | 0.003 |

Abbreviation: CNS, central nervous system.

[a]Defined as being born on the current admission.

[b]See eTable 1 for definitions.

[c]Including ambulatory or outpatient clinics, diagnostic or interventional areas, operating room, postanesthesia recovery room, rehabilitation units, same-day surgical areas, and “other.”

[d]Friday 11 PM to Monday 7 AM

[e]11:00 PM to 6:59 AM

[f]Only including those patients who lost pulse at any time (n = 923 not intubated and n = 908 intubated).