Duration of Cardiopulmonary Resuscitation and Illness Category Impact Survival and Neurologic Outcomes for In-hospital Pediatric Cardiac Arrests

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Background**—**Pediatric cardiopulmonary resuscitation (CPR) for >20 minutes has been considered futile after pediatric in-hospital cardiac arrests. This concept has recently been questioned, although the effect of CPR duration on outcomes has not recently been described. Our objective was to determine the relationship between CPR duration and outcomes after pediatric in-hospital cardiac arrests.

Methods and Results**—**We examined the effect of CPR duration for pediatric in-hospital cardiac arrests from the Get With The Guidelines--Resuscitation prospective, multicenter registry of in-hospital cardiac arrests. We included 3419 children from 328 US and Canadian Get With The Guidelines–Resuscitation sites with an in-hospital cardiac arrest between January 2000 and December 2009. Patients were stratified into 5 patient illness categories: surgical cardiac, medical cardiac, general medical, general surgical, and trauma. Survival to discharge was 27.9%, but only 19.0% of all cardiac arrest patients had favorable neurological outcomes. Between 1 and 15 minutes of CPR, survival decreased linearly by 2.1% per minute, and rates of favorable neurological outcome decreased by 1.2% per minute. Adjusted probability of survival was 41% for CPR duration of 1 to 15 minutes and 12% for >35 minutes. Among survivors, favorable neurological outcome occurred in 70% undergoing <15 minutes of CPR and 60% undergoing CPR >35 minutes. Compared with general medical patients, surgical cardiac patients had the highest adjusted odds ratios for survival and favorable neurological outcomes, 2.5 (95% confidence interval, 1.8–3.4) and 2.7 (95% confidence interval, 2.0–3.9), respectively.

Conclusions**—**CPR duration was independently associated with survival to hospital discharge and neurological outcome. Among survivors, neurological outcome was favorable for the majority of patients. Performing CPR for >20 minutes is not futile in some patient illness categories. **(*Circulation.* 2013;127:442-451.)**

Key Words: cardiopulmonary resuscitation ■ outcome assessment ■ pediatrics ■ resuscitation ■ survival

Cardiac arrests occur in 0.7% to 3% of pediatric hospital admissions and 1.8% to 5.5% of pediatric intensive care unit admissions, representing significant societal, familial, and economic costs.[1–4] Survival rates after in-hospital cardiac arrests (IHCAs) improved from 9% in 1987 to 16% to 30% in the last decade.[1,5–9] Children who undergo cardiac surgery are at greater risk of experiencing a cardiac arrest, although recent studies have found that children with cardiac disease have improved survival compared with other patient groups.[10–12] Conversely, trauma patients have dismal survival rates after cardiac arrest, making it important to consider these distinctions in cardiac arrest research.[13]

Clinical Perspective on p 451

In the mid-1990s, authorities considered pediatric cardiopulmonary resuscitation (CPR) futile beyond 20 minutes duration or when >2 doses of epinephrine were provided.[5,14] Although recent pediatric data indicate that some children survive with CPR of increased duration, this has not been rigorously evaluated.[6,13,15]

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The American Heart Association's Get With The Guidelines–Resuscitation (GWTG-R) is the only national registry of in-hospital resuscitation events. The objectives of this study were to use the GWTG-R data to evaluate the relationship between CPR duration and intact survival to hospital discharge after pediatric IHCA according to patient illness category.

Methods

Design

The AHA GWTG-R is a prospective, multicenter registry of IHCA and resuscitation events using Utstein-style data reporting.[16–18] Its design has been described in detail (www.heart.org/resuscitation).[19,20] This analysis includes data from 328 US and Canadian hospitals between January 1, 2000, and December 31, 2009. This study was approved by the Institutional Review Board at the University of Pittsburgh.

Data Collection and Integrity

Index events are defined as the patient's first cardiopulmonary arrest event during the hospitalization. Predefined patient illness categories are based on patient characteristics at the time of cardiopulmonary arrest. General medical patients had a primary diagnosis of medical illness that was not cardiovascular. Medical cardiac patients had a primary diagnosis of medical illness that was cardiovascular. General surgical patients were preoperative with a general surgical illness or postoperative after noncardiac surgery. Surgical cardiac patients were postoperative after cardiac surgery. Trauma patients had single or multiple injuries. Patients with "do not attempt resuscitation" orders before their first IHCA are excluded from the registry.

Inclusion and Exclusion Criteria

We included all index pulseless IHCA events occurring in patients <18 years of age for which at least 1 minute of chest compressions was provided. In addition to hospital inpatients, we included patients in other locations (outpatient clinics within the hospital, visitors, and inpatients of rehabilitation, skilled nursing, and mental health facilities attached to study hospitals). We excluded patients in whom the event began out of the hospital or in the neonatal intensive care unit, delivery room, or nursery. We also excluded patients with illness categories of newborn, obstetric, or other illnesses. For patients who were documented as receiving >180 minutes of chest compressions, the CPR duration variable was winsorized at a predefined maximum of 180 minutes to reduce the effects of possibly spurious outliers.

Outcome Measures

The primary outcome measure was survival to hospital discharge. Secondary survival measures included return of spontaneous circulation >20 minutes, 24-hour survival, and survival to discharge with favorable neurological outcome. Neurological outcome was determined with the use of pediatric cerebral performance category (PCPC) scales, which were assigned after a review of medical records.[21–23] Favorable neurological outcome was prospectively defined in 2 ways: a PCPC score of 1, 2, or 3 on hospital discharge or discharge PCPC no worse than on admission. Additionally, the analysis was repeated excluding a PCPC score of 3 as a favorable neurological outcome, which can be found in the online-only Data Supplement.

Statistical Analysis

We conducted analyses using SAS 9.0 (SAS Inc, Cary, NC) and Stata 12.1 (Stata Corp, College Station, TX). Chest compression duration was analyzed as both a continuous variable and a categorical variable. Categories of CPR duration were determined with cut points used in previous studies and an analysis of the relationship between hospital survival and duration with a generalized additive model.[1,2,24,25] CPR duration of 15 minutes was chosen as 1 time interval on the basis of previous studies.[1,2,24] The second CPR interval of 35 minutes was based on the slope of the smoothing-spline curve from the generalized additive model, which indicates a change of the relationship between survival and compression duration. Therefore, we studied CPR duration categories of 1 to 15, 16 to 35, and >35 minutes. We used the χ^2 or Fisher exact test for categorical variables and the Wilcoxon rank-sum test, Kruskal-Wallis test, or ANOVA for continuous variables. All *P* values reported are 2 tailed with a significance level set at 0.05. Results are presented as the mean (SD) for symmetrically distributed data and the median (interquartile range) for skewed data. Odds ratios (ORs) are presented with their 95% confidence intervals (CIs). Unadjusted survival and neurological outcome proportions were compared by use of the Fisher exact with Bonferroni correction.

The following variables were selected a priori for the multivariate model because of their clinical significance and on the basis of earlier literature: initial pulseless rhythm, age category, event time of day, event day of week, extracorporeal membrane oxygenation (ECMO), calcium bolus given during the arrest, underlying sepsis, underlying renal insufficiency, and vasoactive infusion when the arrest occurred.[1,13,20,26–28] All remaining variables were tested, and those with a value of $P<0.2$ were added to the model individually. We used the net reclassification index to determine the predictive variables for the final model. We then used the receiver-operating curve and its area under the curve to show that our final model was well suited to predict the probability of survival ($P<0.05$).[29] Multivariable logistic regression models were fit using the data from all study patients to generate the predicted probability of survival and of favorable neurological outcome according to CPR duration for each patient illness category. The variables included in the final survival model were also used in the model predicting neurological outcome. To account for the possible correlation of individual survival in the same hospital, we repeated the analysis using a generalized estimating equation model with the exchangeable correlation structure and with hospital as the cluster variable. The results of this analysis were similar; incorporating hospital effects did not change the conclusion. Adjusted OR comparing illness categories used the general medical patients as the reference group. Predicted probability curves were generated with the adjusted model based on illness categories across CPR duration.

Results

Of 3419 pediatric IHCAs in 328 hospitals that fulfilled inclusion and exclusion criteria (Figure 1 and Figure I in the online-only Data Supplement), 56% occurred in hospitals with ≥80 pediatric beds and 86% occurred in hospitals with at least 20 pediatric beds. The mean±SD age of the study sample was 4.9±6.0 years. Almost all events were witnessed (92.0%) and monitored (90.5%; Table 1). Return of spontaneous circulation for >20 minutes occurred in 2178 patients (64%); 1373 (40%) were still alive at 24 hours after the event; 954 (27.9%) survived to hospital discharge; and 651 (19.0%) had a favorable neurological outcome (68.2% of hospital survivors).

Respiratory insufficiency (59.1%) and hypotension (39.9%) were the most common comorbidities. Among medical and surgical cardiac patients, arrhythmias were present in 29.6% (Table 2). Two thirds of arrests (66.8%) occurred in the intensive care unit, 14.4% in the emergency room, 10.0% on the inpatient ward, and 6.2% in an operative or recovery area (Table 2). Hypotension, arrhythmias, and acute respiratory insufficiency were the most common immediate precipitating causes of the arrests. Variables associated with survival are listed in Table 1, and variables associated with illness categories are listed in Table 2.

Compared with other patients, trauma patients were more likely to be older and their arrests were more likely to occur

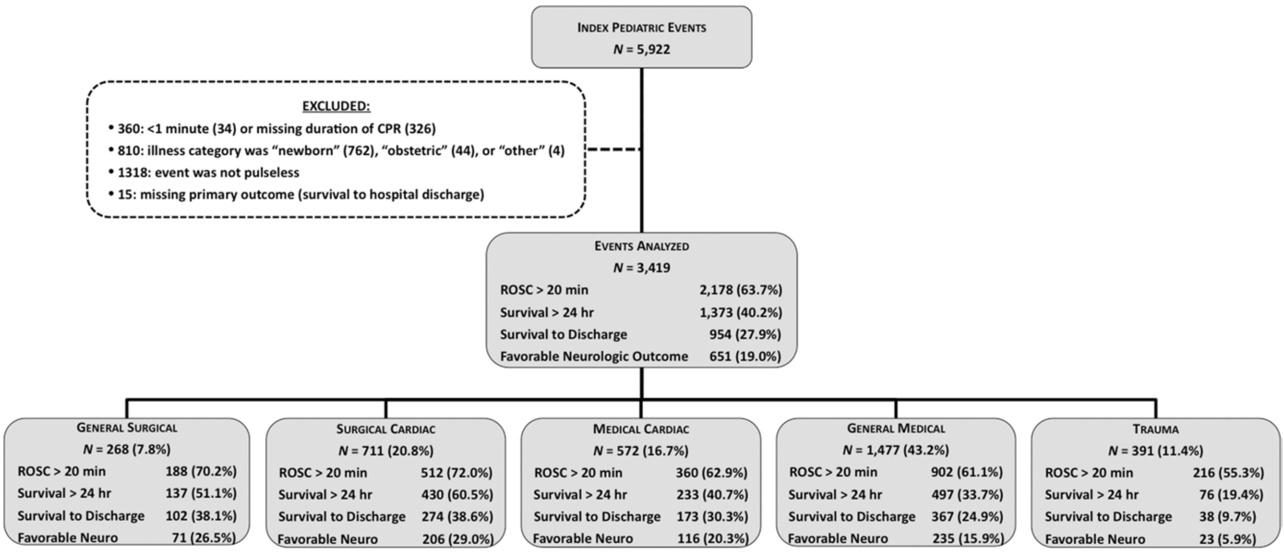

Figure 1. Utstein diagram. CPR indicates cardiopulmonary resuscitation; Neuro, neurological outcome; and ROSC, return of spontaneous circulation.

in the emergency department. Surgical cardiac patients were more likely to be younger and hypotensive, to arrest in an intensive care unit, and to have medical devices and vasoactive infusions in place at the time of the arrest. Both surgical and medical cardiac patients were more likely than other patients to have a shockable first documented rhythm (P<0.0001). Surgical cardiac patients were also placed on ECMO more than any other group, with no change in survival with ECMO (54 of 142 [38.0%] with ECMO and 214 of 544 [39.3%] without ECMO; P=0.776). Favorable neurological outcome for surgical cardiac patients after ECMO was seen in 33 of 123 (26.8%) and in 167 of 503 (33.2%) without ECMO (P=0.174). Among all 227 patients placed on ECMO, survival was not statistically different across CPR duration (from 39.1% after <15 minutes to 33.3% after >35 minutes; P=0.84). However, there was a statistically significant survival benefit for surgical cardiac patients who received >35 minutes of CPR and ECMO (38.5% with ECMO and 16.7% without ECMO; P<0.0001).

Survival to Hospital Discharge

Median duration of CPR for survivors was 10 minutes and for nonsurvivors was 25 minutes (P<0.0001). Among the 954 survivors, 343 (36.0%) had CPR for >15 minutes and 158 (16.6%) had CPR >35 minutes. In the first 15 minutes of CPR, the survival rate fell linearly, decreasing by 2.1% per minute of chest compression (R^2=0.9992). The survival rate continued to decrease with increasing CPR duration: 44.1% for 1 to 15 minutes, 17.8% for 16 to 35 minutes, and 15.9% for >35 minutes. Surgical cardiac patients had the highest percentage of children who had return of spontaneous circulation >20 minutes (72.0%), survival at 24 hours (60.5%), and survival to hospital discharge (38.6%; (Table 3 and Table I in the online-only Data Supplement).

Figure 2 and Figure II in the online-only Data Supplement illustrate the predicted probability of survival according to CPR duration and illness category. Using this adjusted model, we estimate that the probability of survival for similar populations of children who suffer a pulseless cardiac arrest and experience 15 minutes of CPR would be 29.2% and with 35 minutes of CPR would be 19.7%. Figure 3 and Figure III in the online-only Data Supplement show the actual survival and neurological outcomes according to patient illness category for each CPR duration category.

We calculated adjusted ORs according to CPR duration for each patient illness category, and the order of survival was the same as in the unadjusted analysis (Table 4 and Table II in the online-only Data Supplement). Compared with general medical patients, surgical cardiac patients had the best survival (OR, 2.5; 95% CI, 1.8–3.4), followed by general surgical and medical cardiac patients (P<0.0001).

Neurological Outcome

We compared admission and discharge PCPC to evaluate neurological outcome.[22] Similar to survival outcomes, the probability of a favorable neurological outcome fell linearly in the first 15 minutes of CPR (R^2=0.9972) and decreased by 1.2% for each additional minute of chest compressions. Favorable neurological outcome was achieved in 11.0% of all children after CPR for >15 minutes and in 9.5% after 35 minutes. The majority of survivors had a favorable neurological outcome: 223 of 343 (65.0%) after CPR for >15 minutes and 95 of 158 (60.1%) after CPR for >35 minutes.

The predicted probability of a favorable neurological outcome decreased with increasing CPR duration and was affected by illness category (Figure 2 and Figure II in the online-only Data Supplement). Surgical cardiac patients had the highest adjusted predicted probability of a favorable neurological outcome: 38.9% at 15 minutes of CPR and 26.2% at 35 minutes. Medical cardiac, general surgical, and general medical patients had outcomes similar to those of all patients. Trauma patients had the poorest outcomes after any amount of CPR; at 15 minutes, the probability of favorable neurological outcome was 4.3% (2.4% at 35 minutes). At longer durations of CPR, surgical cardiac patients also had the highest probability of a favorable neurological outcome at discharge. At 60 minutes of CPR,

Table 1. Patient Demographics and Arrest Characteristics by Survival to Hospital Discharge

Variable	Subjects, n (%)	Deaths, n (%)
Age category		
0–28 d	649 (19.0)	470 (72.4)
29 d–<12 mo	914 (26.7)	567 (62.0)
12 mo–<8 y	885 (25.9)	660 (74.6)
8–<18 y	971 (28.4)	768 (79.1)
Preexisting conditions		
Respiratory insufficiency	1857 (59.1)	1342 (72.3)
Hypotension	1255 (39.9)	967 (77.1)
Arrhythmia	706 (22.5)	496 (70.3)
Metabolic/electrolyte abnormality	616 (19.6)	493 (80.0)
Baseline depression in CNS function	542 (17.2)	410 (75.7)
Sepsis	462 (14.7)	386 (83.6)
Renal insufficiency	338 (10.8)	286 (84.6)
Pneumonia	301 (9.6)	215 (71.4)
Congestive heart failure, this or prior admission	660 (21.0)	470 (71.2)
Major trauma	365 (11.6)	330 (90.4)
Metastatic or hematologic malignancy	170 (5.4)	153 (90.0)
Acyanotic congenital heart disease	111 (3.5)	61 (55.0)
Cyanotic congenital heart disease	251 (8.0)	158 (63.0)
Hepatic insufficiency	158 (5.0)	137 (86.7)
None	219 (7.0)	156 (71.2)
Patient illness category		
General surgical	268 (7.8)	166 (61.9)
Surgical cardiac	711 (20.8)	437 (61.5)
Medical cardiac	572 (16.7)	399 (69.8)
General medical	1477 (43.2)	1110 (75.2)
Trauma	391 (11.4)	353 (90.3)
Patient type		
Inpatient	2861 (83.7)	2040 (71.3)
Emergency department	496 (14.5)	393 (79.2)
Other locations	62 (1.8)	32 (51.6)
Arrest location		
Intensive care unit	2281 (66.8)	1663 (72.9)
Emergency department	491 (14.4)	389 (79.2)
Inpatient ward	341 (10.0)	225 (66.0)
Other	302 (8.8)	185 (61.3)
Interventions in place before arrest		
Invasive airway	2103 (61.5)	1574 (74.9)
Mechanical ventilation	2108 (61.7)	1593 (75.6)
Vascular access	1931 (56.5)	1428 (74.0)
Vasoactive infusion	1286 (39.4)	1022 (79.5)
Narcotic infusion	298 (9.1)	184 (61.7)
Prehospital arrest	303 (9.7)	274 (90.4)
Immediate cause of arrest*		
Hypotension	1802 (55.2)	1411 (78.3)
Arrhythmia	1623 (49.7)	1159 (71.4)
Acute respiratory insufficiency	1556 (47.7)	1114 (71.6)
Metabolic/electrolyte abnormality	504 (15.4)	417 (82.7)
Inadequate airway	238 (7.3)	114 (47.9)
Acute pulmonary edema	83 (2.5)	72 (86.8)
Hypothermia	65 (2.0)	54 (83.1)
Conscious sedation	32 (1.0)	17 (53.1)
First documented pulseless rhythm		
Asystole	1265 (37.7)	966 (39.9)
Pulseless electric activity	1205 (35.9)	847 (35.0)
Ventricular fibrillation	265 (7.9)	188 (7.8)
Ventricular tachycardia	168 (5.0)	115 (4.8)
Weekend	1031 (34.0)	785 (76.1)
Night	1028 (30.1)	766 (74.5)
Category of CPR duration, min		
1–15	1386 (40.5)	775 (55.9)
16–35	1037 (30.3)	852 (82.2)
>35	996 (29.1)	838 (84.1)
Witnessed or monitored	3286 (96.1)	2356 (71.7)
Pharmacological interventions		
Epinephrine bolus	3041 (88.9)	2331 (76.7)
Sodium bicarbonate	2135 (62.5)	1719 (80.5)
Calcium chloride or gluconate	1646 (48.2)	1327 (80.6)
Fluid bolus	1379 (40.4)	1084 (78.6)
Extracorporeal membrane oxygenator	227 (6.7)	149 (65.6)
Total	3419 (100)	2465 (100)

CNS indicates central nervous system; and CPR, cardiopulmonary resuscitation. Night is defined as 11 PM to 6:59 AM. Weekend is defined as 11 PM Friday to 6:59 AM Monday.

*Patients could have >1 immediate cause of arrest.

the adjusted probability of favorable neurological outcome was 14.6%, and at 90 minutes, it was 6.7%.

Adjusted ORs for favorable neurological outcome are reported in Table 4 and Table II in the online-only Data Supplement. Compared with general medical patients, surgical cardiac patients had the highest odds of achieving a favorable neurological outcome (OR, 2.7; 95% CI, 2.0–3.9; P<0.001). Trauma patients were the only group to have decreased odds of favorable neurological outcome compared with the general medical group (OR, 0.2; 95% CI, 0.1–0.4; P<0.001). When we redefined favorable neurological outcome as PCPC 1 or 2 or no change from baseline, we also found similar results in all illness categories (see the online-only Data Supplement).

Discussion

This is the largest study of pediatric IHCAs to date with a large, multicenter sample that is widely generalizable. We found that after adjustment for confounding factors, CPR duration was inversely associated with survival to hospital discharge and neurological outcome, and that the sample of surgical cardiac patients had better outcomes than patients in all other illness categories. Importantly, this study suggests that some children who would presumably die without CPR survive with a favorable neurological outcome even after prolonged resuscitation efforts.

Table 2. Patient Demographics and Arrest Characteristics by Patient Illness Category

Characteristic	General Surgical (n=268)	Surgical Cardiac (n=711)	Medical Cardiac (n=572)	General Medical (n=1477)	Trauma (n=391)	All Patients (n=3419)
Age category, n (%)						
0–28 d	43 (16.0)	354 (49.8)	101 (17.7)	146 (9.9)	5 (1.3)	649 (19.0)
29 d–<12 mo	77 (28.7)	204 (28.7)	190 (33.2)	408 (27.6)	35 (9.0)	914 (26.7)
12 mo–<8 y	62 (23.1)	96 (13.5)	159 (27.8)	455 (30.8)	113 (28.9)	885 (25.9)
8 y–<18 y	86 (32.1)	57 (8.0)	122 (21.3)	468 (31.7)	238 (60.9)	971 (28.4)
Preexisting conditions, n (%)						
Respiratory insufficiency	145 (60.2)	409 (60.2)	290 (54.3)	849 (63.3)	164 (47.1)	1857 (59.1)
Hypotension	94 (39.0)	360 (52.9)	176 (33.0)	461 (34.4)	164 (47.1)	1255 (39.9)
Arrhythmia	35 (14.5)	209 (30.7)	171 (32.0)	227 (16.9)	64 (18.4)	706 (22.5)
Metabolic abnormality	45 (18.7)	110 (16.2)	83 (15.5)	315 (23.5)	63 (18.1)	616 (19.6)
Baseline depression in CNS function	46 (19.1)	26 (3.8)	51 (9.6)	343 (25.6)	76 (21.8)	542 (17.2)
Sepsis	32 (13.3)	56 (8.2)	61 (11.4)	302 (22.5)	11 (3.2)	462 (14.7)
Renal insufficiency	25 (10.4)	60 (8.8)	48 (9.0)	189 (14.1)	16 (4.6)	338 (10.8)
Pneumonia	10 (4.2)	19 (2.8)	43 (8.1)	219 (16.3)	10 (2.9)	301 (9.6)
CHF, this or prior admission	13 (5.4)	311 (45.7)	245 (45.9)	88 (6.6)	3 (0.9)	660 (21.0)
Major trauma	15 (6.2)	1 (0.2)	5 (0.9)	22 (1.6)	322 (92.5)	365 (11.6)
Metastatic or hematologic malignancy	11 (4.6)	3 (0.4)	9 (1.7)	146 (10.9)	1 (0.3)	170 (5.4)
Acyanotic CHD	7 (2.9)	68 (10.0)	20 (3.8)	16 (1.2)	0 (0)	111 (3.5)
Cyanotic CHD	1 (0.4)	179 (26.3)	60 (11.2)	11 (0.8)	0 (0)	251 (8,0)
Hepatic insufficiency	26 (10.8)	23 (3.4)	15 (2.8)	86 (6.4)	8 (2.3)	158 (5.0)
None	21 (8.7)	13 (1.9)	50 (9.4)	121 (9.0)	14 (4.0)	219 (7.0)
Patient type, n (%)						
Inpatient	258 (96.3)	698 (98.2)	444 (77.6)	1184 (80.2)	277 (70.8)	2861 (83.7)
Emergency department	4 (1.5)	3 (0.4)	106 (18.5)	272 (18.4)	111 (28.4)	496 (14.5)
Other locations	6 (2.2)	10 (1.4)	22 (3.9)	21 (1.4)	3 (0.8)	62 (1.8)
Arrest location, n (%)						
Intensive care unit	164 (61.2)	614 (86.4)	350 (61.3)	921 (62.5)	232 (59.3)	2281 (66.8)
Emergency department	4 (1.5)	3 (0.4)	104 (18.2)	274 (18.6)	106 (27.1)	491 (14.4)
Inpatient ward	35 (13.1)	33 (4.6)	53 (9.3)	212 (14.4)	8 (2.1)	341 (10.0)
Other*	65 (24.3)	61 (8.6)	64 (11.2)	67 (4.6)	45 (11.5)	302 (8.8)
Interventions in place at arrest, n (%)						
Invasive airway	173 (64.6)	522 (73.4)	265 (46.3)	821 (55.6)	322 (82.4)	2103 (61.5)
Mechanical ventilation	168 (62.7)	521 (73.3)	281 (49.1)	823 (55.7)	315 (80.6)	2108 (61.7)
Vascular access†	162 (60.5)	401 (56.4)	318 (55.6)	811 (54.9)	239 (61.1)	1931 (56.5)
Vasoactive infusion	73 (28.6)	434 (62.9)	187 (34.2)	439 (31.2)	153 (41.6)	1286 (39.4)
Narcotic infusion	24 (9.4)	139 (20.1)	28 (5.1)	94 (6.7)	13 (3.5)	298 (9.1)
Prehospital arrest, n (%)	14 (5.8)	14 (2.2)	54 (10.2)	126 (9.3)	95 (26.8)	303 (9.7)
Weekend, n (%)	65 (27.7)	171 (26.5)	176 (34.7)	464 (35.4)	155 (46.4)	1031 (34.0)
Night, n (%)	67 (25.0)	205 (28.8)	169 (29.6)	454 (30.7)	133 (34.0)	1028 (30.1)
Hospital characteristics, n (%)						
Facility beds, n						
<300	70 (28.3)	197 (29.1)	144 (26.8)	389 (28.3)	41 (11.5)	841 (26.3)
300–499	91 (36.8)	203 (29.9)	213 (39.7)	571 (41.5)	166 (46.5)	1244 (38.9)
≥500	86 (34.8)	278 (41.0)	180 (33.5)	417 (30.3)	150 (42.0)	1111 (34.8)
Pediatric intensive care unit beds, n						
0	12 (5.2)	16 (2.6)	76 (15.1)	181 (13.8)	94 (27.4)	379 (12.6)
<10	22 (9.5)	15 (2.4)	44 (8.8)	142 (10.9)	49 (14.3)	272 (9.0)
10–19	58 (25.1)	138 (22.0)	113 (22.5)	316 (24.2)	75 (21.9)	700 (23.3)

(Continued)

Table 2. Continued

Characteristic	General Surgical (n=268)	Surgical Cardiac (n=711)	Medical Cardiac (n=572)	General Medical (n=1477)	Trauma (n=391)	All Patients (n=3419)
≥20	139 (60.2)	457 (73.0)	269 (53.6)	669 (51.2)	125 (36.4)	1659 (55.1)
Teaching hospital	227 (91.9)	661 (97.5)	478 (89.0)	1210 (87.9)	323 (90.5)	2899 (90.7)
Immediate cause of arrest, n (%)‡						
Hypotension	132 (52.4)	448 (64.9)	279 (51.0)	702 (50.0)	241 (65.0)	1802 (55.2)
Arrhythmia	109 (43.3)	375 (54.3)	327 (59.8)	611 (43.5)	201 (54.2)	1623 (49.7)
Acute respiratory insufficiency	112 (44.4)	247 (35.8)	256 (46.8)	803 (57.2)	138 (37.2)	1556 (47.7)
Metabolic/electrolyte abnormality	38 (15.1)	75 (10.9)	60 (11.0)	264 (18.8)	67 (18.1)	504 (15.4)
Inadequate airway	36 (14.3)	34 (4.9)	25 (4.6)	124 (8.8)	19 (5.1)	238 (7.3)
Acute pulmonary edema	4 (1.6)	12 (1.7)	15 (2.7)	41 (2.9)	11 (3.0)	83 (2.5)
Hypothermia	4 (1.6)	8 (1.2)	9 (1.7)	26 (1.9)	18 (4.9)	65 (2.0)
Conscious sedation	4 (1.6)	5 (0.7)	7 (1.3)	13 (0.9)	3 (0.8)	32(1.0)
First documented pulseless rhythm, n (%)						
Asystole	112 (42.6)	169 (24.1)	206 (36.4)	661 (45.2)	129 (33.1)	1277 (37.8)
Pulseless electrical activity	88 (33.5)	319 (45.6)	179 (31.6)	462 (31.6)	164 (42.1)	1212 (35.8)
Ventricular fibrillation	12 (4.6)	80 (11.4)	68 (12.0)	69 (4.7)	36 (9.2)	265 (7.8)
Ventricular tachycardia	6 (2.3)	39 (5.6)	37 (6.5)	59 (4.0)	28 (7.2)	169 (5.0)
Duration of CPR, median (25%, 75% IQR), min						
All patients	19 (8, 37)	25 (9, 50)	23 (10, 43)	21 (10, 39)	14 (7, 27)	20 (9, 40)
Survivors	8 (3–15)	11 (5–32)	12 (4–33)	10 (4–21)	8.5 (3–17)	10 (4–25)
Nonsurvivors	28 (14–45)	33 (15–57)	27 (16–50)	25 (13–45)	15 (7–28)	25 (12–45)
Category of CPR duration, n (%)						
1–15 min	124 (46.3)	272 (38.3)	196 (34.3)	583 (39.5)	211 (54.0)	1386 (40.5)
16–35 min	74 (27.6)	172 (24.2)	196 (34.3)	480 (32.5)	115 (29.4)	1037 (30.3)
>35 min	70 (26.1)	267 (37.6)	180 (31.5)	414 (28.0)	65 (16.6)	996 (29.1)
Reason resuscitation ended, n (%)						
Survived, ROC	176 (65.7)	480 (67.5)	317 (55.4)	789 (53.4)	187 (47.8)	1949 (57.0)
Died, no ROC	75 (28.0)	190 (26.7)	208 (36.4)	543 (36.8)	157 (40.2)	1173 (34.3)
Died, medical futility	8 (3.0)	26 (3.7)	33 (5.8)	80 (5.4)	39 (10.0)	186 (5.4)
Died, advance directive/family§	9 (3.4)	15 (2.1)	14 (2.4)	65 (4.2)	8 (2.1)	111 (3.3)
Witnessed/monitored, n (%)	262 (97.8)	708 (99.6)	535 (93.5)	1397 (94.6)	384 (98.2)	3286 (96.1)
Pharmacological interventions, n (%)						
Epinephrine bolus†	228 (85.1)	636 (89.5)	501 (87.6)	1317 (89.2)	359 (91.8)	3041 (88.9)
Sodium bicarbonate	156 (58.2)	497 (69.9)	375 (65.6)	898 (60.8)	209 (53.5)	2135 (62.5)
Calcium chloride or gluconate	122 (45.5)	469 (66.0)	277 (48.4)	649 (44.0)	129 (33.0)	1646 (48.2)
Fluid bolus†	102 (38.1)	288 (40.5)	226 (39.5)	596 (40.4)	167 (42.7)	1379 (40.4)
ECMO, n (%)	10 (3.8)	142 (20.7)	41 (7.2)	34 (2.3)	0 (0)	227 (6.7)

CHD indicates congenital heart disease; CHF, congestive heart failure; CNS, central nervous system; ECMO, extracorporeal membrane oxygenator; IQR, interquartile range; and ROC, return of circulation. Night is defined as 11 PM to 6:59 AM. Weekend is defined as 11 PM Friday to 6:59 AM Monday.

*Other includes operating room, recovery, and diagnostic areas.

†Insignificant. All *P* values were statistically significant at <0.01 except where noted.

‡Patients could have >1 immediate cause of arrest.

§Patients with advanced directives or "do not resuscitate" (DNR) orders preceding an arrest were excluded from the registry, but patients whose families created a DNR order after their arrest are included.

Several studies found CPR duration to be a key predictor of survival after cardiac arrest. However, many studies were single-center studies, focused on out-of-hospital arrests (or both IHCA and out-of-hospital arrests), or used retrospectively collected data.[15,24,30] Inclusion of adults, smaller sample sizes, and inconsistent definitions also made it difficult to quantify the true impact of CPR duration and patient illness category in these studies. However, our study used prospectively collected data from multiple centers using the Utstein guidelines for uniform data reporting, carefully minimizing information bias, observer bias, and surveillance bias.

We analyzed outcomes after CPR durations of 1 to 15, 16 to 35, and >35 minutes, with each duration having progressively

Table 3. Primary and Secondary Outcomes by Patient Illness Category

Characteristic	General Surgical (n=268), n (%)	Surgical Cardiac (n=711), n (%)	Medical Cardiac (n=572) , n (%)	General Medical (n=1477), n (%)	Trauma (n=391), n (%)	All Patients (n=3419), n (%)
Survival outcomes						
Survived to discharge	102 (38.1)	274 (38.6)	173 (30.3)	367 (24.9)	38 (9.7)	954 (27.9)
ROSC >20 min	188 (70.2)	512 (72.0)	360 (62.9)	902 (61.1)	216 (55.3)	2178 (63.7)
Survived at 24 h	137 (51.1)	430 (60.5)	233 (40.7)	497 (33.7)	76 (19.4)	1373 (40.2)
Neurological outcome						
Favorable*	71 (26.5)	206 (29.0)	116 (20.3)	235 (15.9)	23 (5.9)	651 (19.0)
Poor	175 (65.3)	445 (62.6)	409 (71.5)	1144 (77.5)	357 (91.3)	2530 (74.0)
Unknown	22 (8.2)	60 (8.4)	47 (8.2)	98 (6.6)	11 (2.8)	238 (7.0)

ROSC indicates return of spontaneous circulation.

All *P* values were statistically significant at <0.01.

*Favorable neurological outcome was defined as pediatric cerebral performance category of 1, 2, or 3 on hospital discharge or no change from baseline.

worse survival. Previous studies used 15 minutes as the initial cut point. We found that outcomes in the first 15 minutes are linear and decline rapidly, highlighting the importance of quick return of spontaneous circulation. Each minute is critical to achieving both survival and a favorable neurological outcome. However, the finding that intact survival after >35 minutes of CPR is as high as 16.2% in certain patient groups is novel, considering that some studies have found overall survival to be 16%.

The survival outcomes in this sample are similar to recent studies of pediatric IHCA.[1,6–9] Other studies also reported favorable neurological survival to be 14% to 22%,[1,6,7,27] which is consistent with the 19.0% rate of survival with favorable neurological outcome and 68.2% rate of favorable neurological outcomes among hospital survivors reported in this study.[9]

There are many reasons why CPR duration could affect survival and neurological outcomes after IHCA. Even when ideally performed, CPR still represents a low-flow state, and increased duration of CPR increases the risk of interruptions from changes in providers and leads to a longer duration of no flow.[31] Longer duration of CPR has also been associated with shallower chest compressions and excessive residual leaning force, which contribute to worse perfusion of heart and brain.[32] Nevertheless, prolonged duration of CPR was able to bridge many patients from pulselessness to return of spontaneous circulation and survival to discharge with a favorable neurological outcome. Although these data indicate that prolongation of CPR leads to worse outcomes, they also indicate that some children have a favorable neurological outcome even after prolonged CPR. Unfortunately, these data do not provide a simple solution for when to discontinue CPR.

The finding that patient illness category is strongly associated with mortality is consistent with previous reports. Studies of both adults and children reported higher survival rates in cardiac intensive care units than in noncardiac units, which suggests a survival benefit for cardiac patients.[11,33] A multicenter study by Berens et al[34] involving 257 pediatric cardiac arrests found that patients with respiratory-induced arrest had a better survival at shorter CPR durations but that survival decreased dramatically with time, whereas survival after a cardiac-induced arrest remained unchanged with increasing duration of CPR. More recently, GWTG-R investigators reported that pediatric surgical cardiac patients are more likely to survive to hospital discharge after IHCA than those with medical cardiac or noncardiac disease.[10] Similarly, the results of our analysis suggest that the probability of survival with favorable neurological outcome in surgical cardiac patients who undergo long durations of CPR may be higher than in other categories of illness, which may allow clinicians to estimate outcomes for these patients after arrest.

We found that surgical cardiac patients had the best outcomes and trauma patients had the worst outcomes at each incremental increase in CPR duration. In fact, surgical cardiac patients had a better probability of survival after 90 minutes of chest compressions than trauma patients had after 1 minute. The reasons for this difference are likely multifactorial.

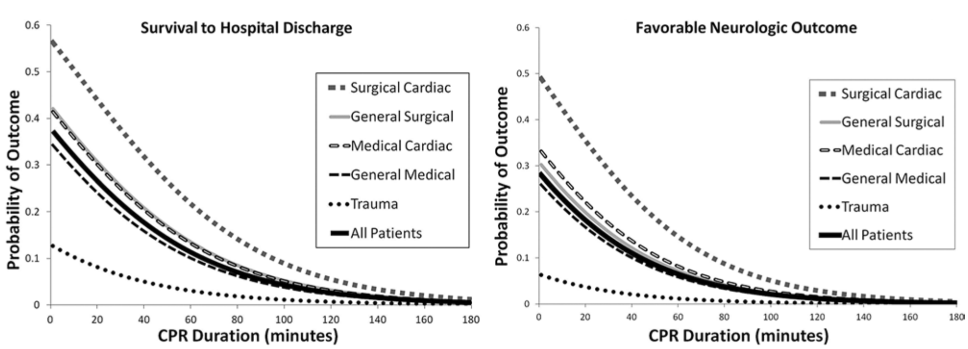

Figure 2. Adjusted probability of outcomes at hospital discharge by cardiopulmonary resuscitation (CPR) duration stratified by patient illness category (adjusted for initial pulseless rhythm, age category, weekend, night, extracorporeal membrane oxygenation, calcium administration, sepsis, renal insufficiency, vasoactive infusion during arrest, event location, sodium bicarbonate administration, prior history of a cardiopulmonary arrest, prearrest apnea monitor, prearrest pulse oximeter, and patient hypotension before arrest).

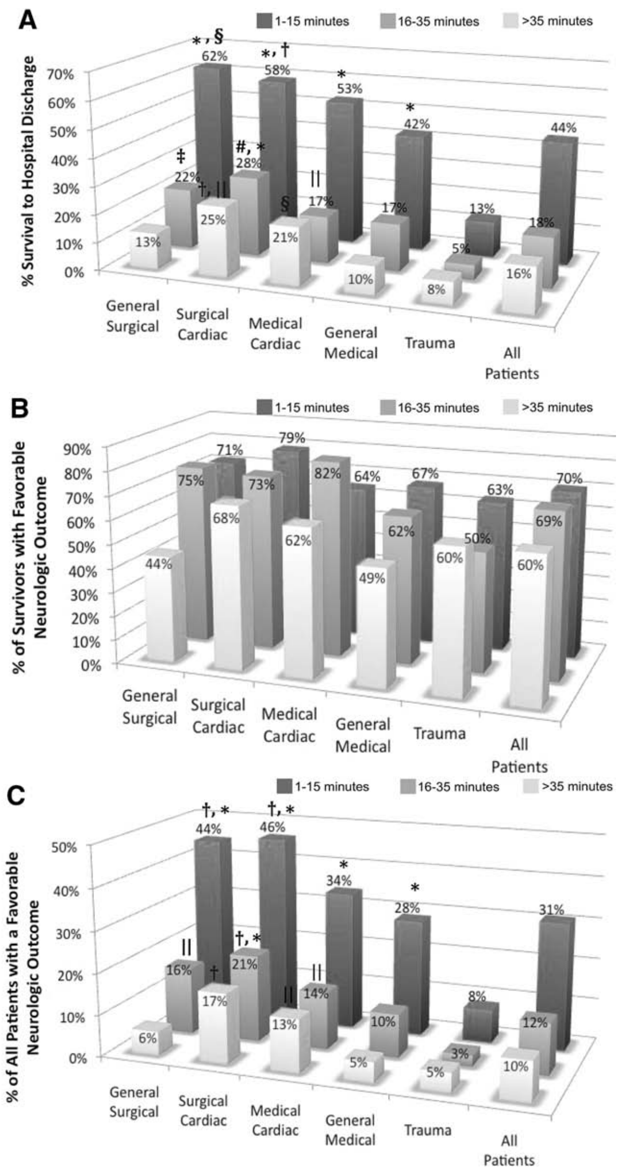

Figure 3. Proportion of **(A)** all patients with survival to hospital discharge, **(B)** survivors with favorable neurological outcome, and **(C)** all patients with favorable neurological outcome according to patient illness category and cardiopulmonary resuscitation duration, unadjusted.
*P<0.001 vs trauma group
†P<0.001 vs general medical group
‡P<0.01 vs trauma
§P<0.01 vs general medical
‖P<0.05 vs trauma
#P<0.05 vs general medical

Although cardiac patients in this study were younger and more frequently had shockable rhythms (both previously associated with higher survival),[6,7,27] we attempted to control for these factors in the multivariate model. In addition to the younger age of the surgical cardiac sample, some key variables of the surgical cardiac patients not recorded in the registry may explain the difference in outcomes. Furthermore, the baseline risk of surgical cardiac patients may be modified by characteristics related to their postsurgical condition. For example, mechanisms involved such as preconditioning may be cardioprotective in subsequent ischemia,[35,36] and postbypass surgical cardiac patients may be preconditioned to better withstand the low-flow, hypoxic conditions of an arrest.

All studies of multicenter registries are limited by the challenges of ensuring data integrity at multiple sites. These limitations were minimized by the rigorous abstractor certification process, uniform data collection, and use of consistent Utstein definitions. Another potential limitation of this study is lack of generalizability. The GWTG-R centers account for 10% of all hospitals in the United States and represent all geographic US Census regions. However, these volunteer centers pay a fee and thus may have more resources, as well as a greater interest in CPR outcomes, than other US hospitals. Thus, the absolute proportion rates in our sample population may differ from those in other US hospitals, although this may not affect the relative proportions. In addition, we excluded infants cared for in the neonatal intensive care unit, including surgical cardiac or general surgical patients; therefore, these results would not be generalizable to this population. This study is also limited by the potential heterogeneity of the illness categories, which do not indicate the cause of arrest. We were unable to completely control for disease severity through the use of physiological variables (an innate limitation of the GWTG-R registry). However, this database did have >400 variables that we were able to evaluate and include in our assessment. This study may also have limitations in patient selection. We included outpatients and visitors (n=62) in this study because the arrests occurred in a hospital where responders are rapidly present with in-hospital expertise and equipment. However, these patients are undoubtedly different from inpatient or emergency room patients, and the results may not be generalizable to this group. We also included patients with a history of an arrest during a previous admission (n=134), which could have the remote possibility that some of these patients were included in the analysis more than once. Although the probability is low, we included prior cardiopulmonary arrest in the multivariable model to adjust for some of these limitations. Finally, our study is limited by lack of long-term neurological follow-up and the use of only a global measure of neurological function, the PCPC, as a neurological outcome. However, previous studies suggest that neurological status at discharge is not substantially different from status at 6 months and 1 year after arrest, and the PCPC is the standard for Utstein reporting.[1,37,38]

These findings have implications for in-hospital care. Pediatric providers involved with inpatient resuscitation should understand that rapid deployment of high-quality life support is essential because the probability of survival and favorable neurological outcome decreases with every passing minute. This study should also help dispel common perceptions that CPR is futile beyond 20 minutes because patients in certain illness categories such as surgical cardiac patients have favorable probabilities of good neurological survival after longer durations of CPR. Conversely, trauma patients who sustain IHCA have much worse outcomes across all CPR durations, which is consistent with previous studies.[13,39] Although this study was not designed to offer decision rules about when to discontinue CPR in individual patients, the results suggest that further studies are indicated to determine whether prolonged resuscitative efforts are warranted in particular groups of patients such as posttraumatic arrests.

Table 4. Adjusted Odds Ratios by Patient Illness Category

	Survival to Hospital Discharge			Favorable Neurological Outcome at Hospital Discharge		
	Adjusted Odds Ratio (95% CI)*			Adjusted Odds Ratio (95% CI)*		
	1–15 min	16–35 min	36–180 min	1–15 min	16–35 min	36–180 min
Surgical cardiac	3.34 (2.10–5.34)	2.00 (1.07–3.75)	2.13 (1.07–4.25)	2.92 (1.79–4.76)	2.20 (1.09–4.44)	3.74 (1.59–8.82)
Medical cardiac	1.63 (1.05–2.53)	0.82 (0.47–1.44)	2.18 (1.15–4.13)	1.29 (0.81–2.07)	1.05 (0.56–1.95)	3.21 (1.44–7.12)
General surgical	1.31 (0.75–2.30)	1.93 (0.88–4.24)	1.10 (0.39–3.12)	1.03 (0.58–1.85)	1.96 (0.82–4.72)	1.30 (0.36–4.73)
General medical	1	1	1	1	1	1
Trauma	0.29 (0.16–0.50)	0.16 (0.05–0.49)	0.40 (0.09–1.84)	0.21 (0.11–0.42)	0.12 (0.03–0.54)	†
P	<0.0001	0.0005	0.0377	<0.0001	0.0040	0.0175

CI indicates confidence interval.

*The adjusted model includes initial pulseless rhythm, age category, weekend, night, extracorporeal membrane oxygenation, calcium administration, sepsis, renal insufficiency, vasoactive infusion during arrest, event location, sodium bicarbonate administration, prior history of a cardiopulmonary arrest, prearrest apnea monitor, prearrest pulse oximeter, and patient hypotension prior to arrest.

†Too few cases to report (3 of 65 had favorable neurological outcome in trauma category).

Conclusions

We found that CPR duration was inversely associated with survival to hospital discharge and neurological outcome, even after adjustment for confounding factors. Surgical cardiac patients had improved outcomes compared with patients in all other illness categories. Importantly, this study suggests that a proportion of children who would presumably die without CPR survive with a favorable neurological outcome even after prolonged CPR.

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Disclosures

Part of the content of this manuscript was presented in poster format at the 40th Annual Critical Care Congress; January 2011; San Diego, CA. The Scientific Advisory Board of the AHA provided review and approval of the manuscript, and the Executive Database Steering Committee of the AHA provided additional peer review of the manuscript.

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CLINICAL PERSPECTIVE

This study analyzes data from a large, national registry of cardiopulmonary resuscitation (CPR) process of care and outcomes to show that outcomes are best with shorter durations of CPR and that many children survive after prolonged CPR (>35 minutes of CPR). Practicing clinicians who have the potential to care for children (even unexpectedly) should appreciate the potential for good outcomes after prolonged CPR in children, especially among certain patient groups. In addition, these data strongly support the importance of initial effective CPR to increase the likelihood of return of spontaneous circulation promptly, which in turn is associated with a greater likelihood of survival to discharge. The majority of pulseless cardiac arrest survivors in this study had good neurological outcomes even after prolonged CPR, which contradicts previous notions that CPR is futile after 20 minutes.

Circulation

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Duration of Cardiopulmonary Resuscitation and Illness Category Impact Survival and Neurologic Outcomes for In-hospital Pediatric Cardiac Arrests

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SUPPLEMENTAL MATERIAL

SUPPLEMENTAL METHODS:

The Methods for the Supplement are the same as in the original manuscript except for the subsection below.

Outcome Measures

The primary outcome measure was survival to hospital discharge. Secondary survival measures included return of spontaneous circulation (ROSC) >20 minutes, 24-hour survival, and survival to discharge with favorable neurologic outcome. Neurologic outcome was determined using pediatric cerebral performance category (PCPC) scales, which were assigned based on review of medical records.[21-23] Favorable neurologic outcome was prospectively defined in two ways; 1) PCPC score of 1 or 2 on hospital discharge, or 2) Discharge PCPC no worse than on admission.

SUPPLEMENTAL TABLES:

SUPPLEMENTAL TABLE I. Primary and Secondary Outcomes by Patient Illness Category

Characteristic	General Surgical *(n=268)*	Surgical Cardiac *(n=711)*	Medical Cardiac *(n=572)*	General Medical *(n=1477)*	Trauma *(n=391)*	All Patients *(n=3419)*
Survival Outcomes, *n* (%)						
Survived to discharge	102 (38.1)	274 (38.6)	173 (30.3)	367 (24.9)	38 (9.7)	954 (27.9)
ROSC >20 minutes	188 (70.2)	512 (72.0)	360 (62.9)	902 (61.1)	216 (55.3)	2178 (63.7)
Survived at 24 hours	137 (51.1)	430 (60.5)	233 (40.7)	497 (33.7)	76 (19.4)	1373 (40.2)
Neurologic Outcome, *n* (%)						
Favorable*	66 (24.6)	196 (27.6)	114 (19.9)	227 (15.4)	21 (5.4)	624 (18.3)
Poor	180 (67.2)	455 (64.0)	411 (71.9)	1152 (78.0)	359 (91.8)	2557 (74.8)
Unknown	22 (8.2)	60 (8.4)	47 (8.2)	98 (6.6)	11 (2.8)	238 (7.0)

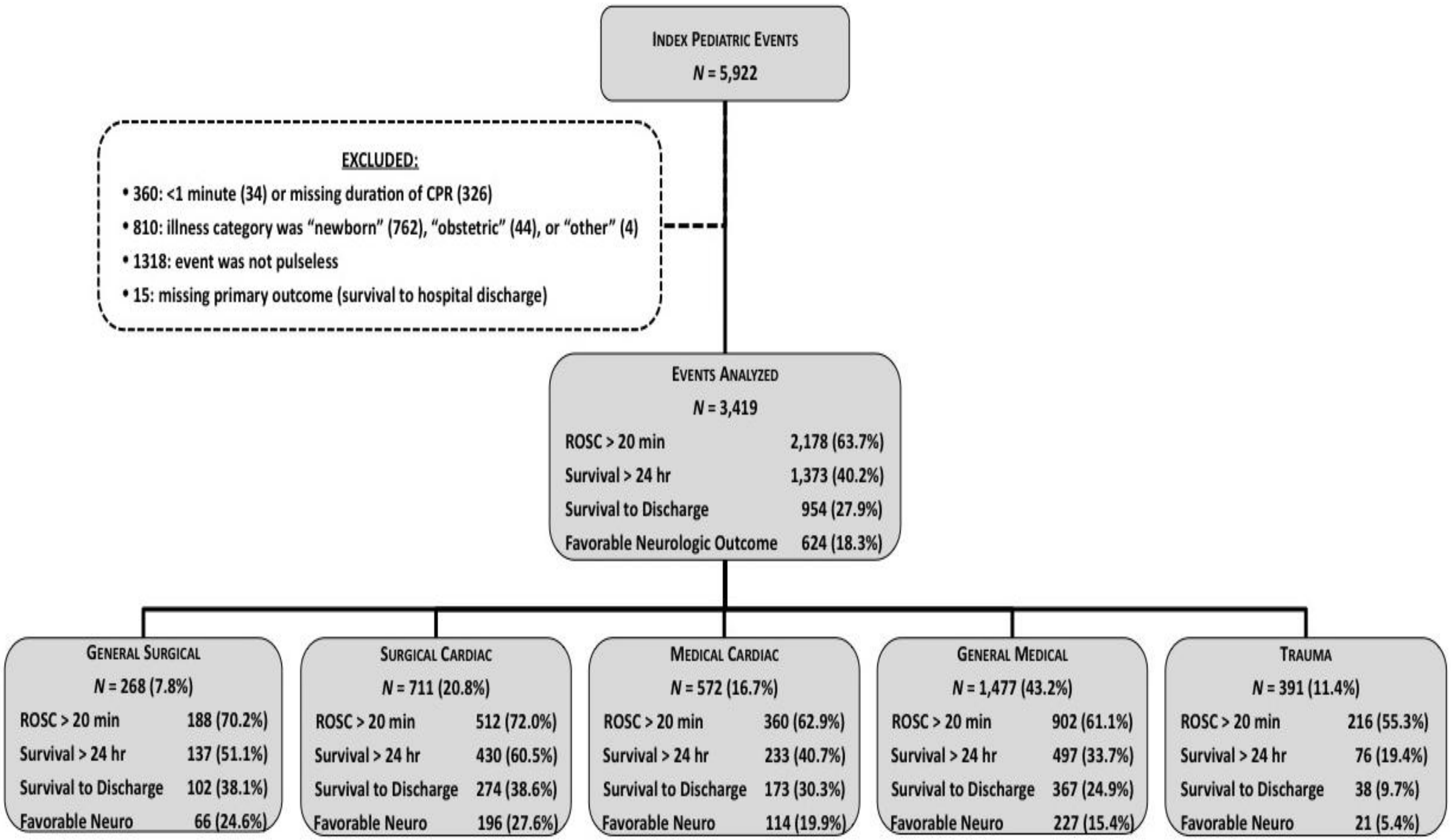
All p-values were statistically significant at <0.01. **ROSC**, return of spontaneous circulation. *Favorable neurologic outcome was defined as Pediatric Cerebral Performance Category of 1 or 2 upon hospital discharge, or no change from baseline.

SUPPLEMENTAL TABLE II. Adjusted Odds Ratios by Patient Illness Category

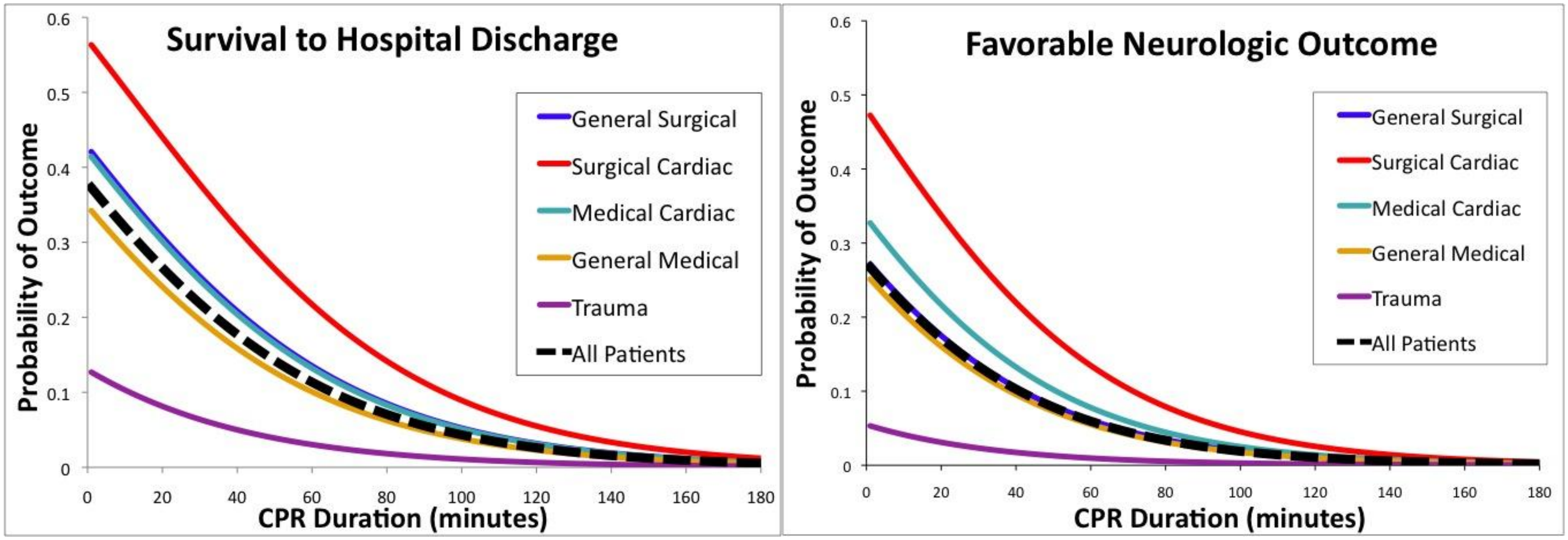
	Survival to Hospital Discharge Adjusted Odds Ratio (95% CI)*			Favorable Neurologic Outcome at Hospital Discharge Adjusted Odds Ratio (95% CI)*		
	1-15 minutes	**16-35 minutes**	**36-180 minutes**	**1-15 minutes**	**16-35 minutes**	**36-180 minutes**
Surgical Cardiac	3.34 (2.10-5.34)	2.00 (1.07-3.75)	2.13 (1.07-4.25)	2.69 (1.66-4.36)	2.26 (1.11-4.60)	4.07 (1.68-9.87)
Medical Cardiac	1.63 (1.05-2.53)	0.82 (0.47-1.44)	2.18 (1.15-4.13)	1.38 (0.86-2.21)	1.05 (0.56-1.96)	2.99 (1.32-6.79)
General Surgical	1.31 (0.75-2.30)	1.93 (0.88-4.24)	1.10 (0.39-3.12)	0.92 (0.52-1.64)	1.97 (0.82-4.75)	0.86 (0.20-3.67)
General Medical	1	1	1	1	1	1
Trauma	0.29 (0.16-0.50)	0.16 (0.05-0.49)	0.40 (0.09-1.84)	0.20 (0.10-0.41)	0.05 (0.01-0.43)	†
***p*-value**	<0.0001	0.0005	0.0377	<0.0001	0.0044	0.0135

CI, confidence interval. *The adjusted model includes: initial pulseless rhythm, age category, weekend, night, extracorporeal membrane oxygenation, calcium administration, sepsis, renal insufficiency, vasoactive infusion during arrest, event location, sodium bicarbonate administration, prior history of a cardiopulmonary arrest, pre-arrest apnea monitor, pre-arrest pulse oximeter, and patient hypotension prior to arrest. †, Too few cases to report (3 of 65 had favorable neurologic outcome in trauma category).

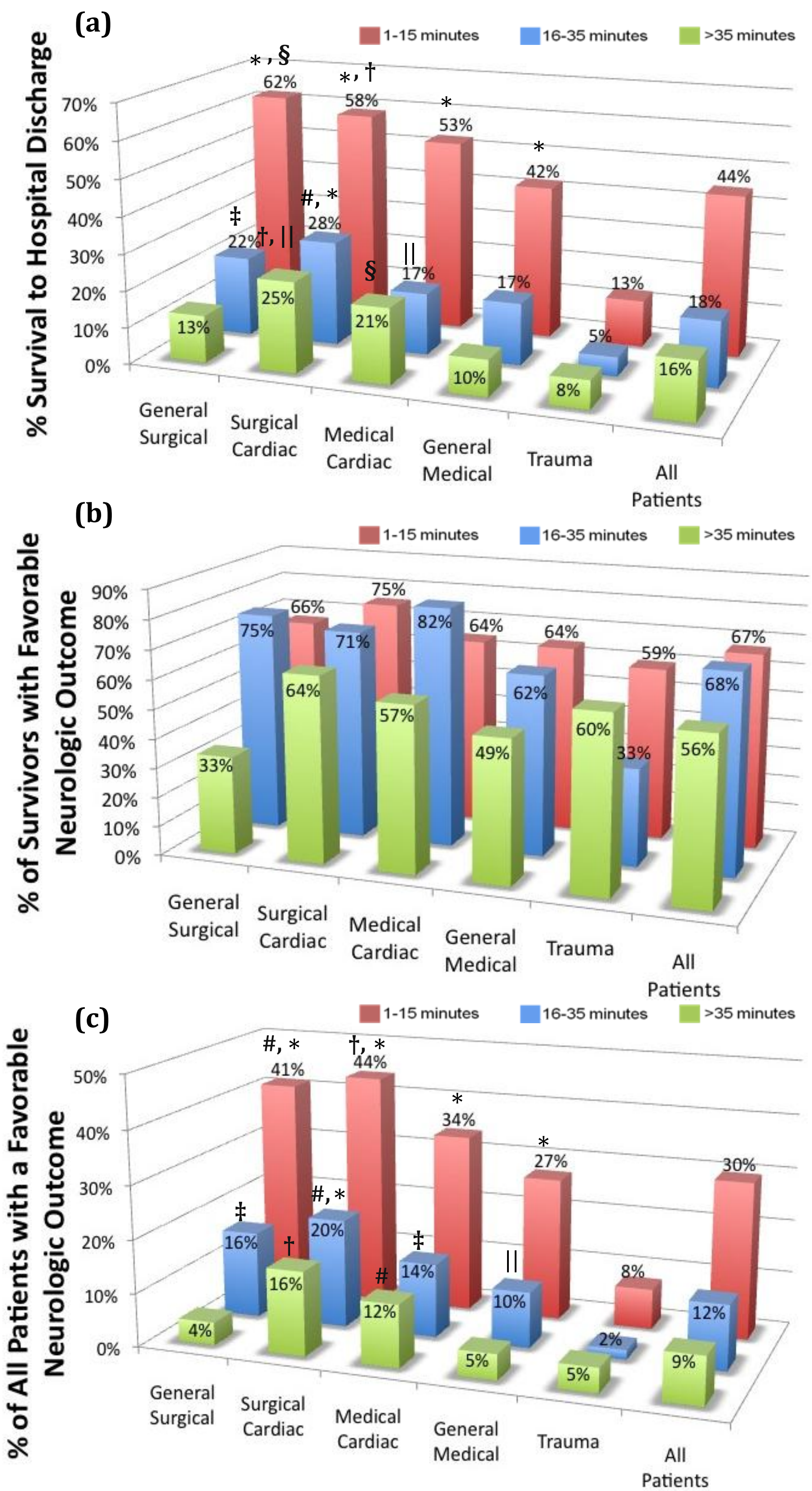
SUPPLEMENTAL FIGURES:



SUPPLEMENTAL FIGURE I.



SUPPLEMENTAL FIGURE II.



SUPPLEMENTAL FIGURE III.

SUPPLEMENTAL FIGURE LEGENDS:

SUPPLEMENTAL FIGURE I. Utstein diagram. *ROSC*, return of spontaneous circulation; *min*, minutes; *hr*, hours; *Neuro*, neurologic outcome.

SUPPLEMENTAL FIGURE II. Adjusted Probability of Outcomes at Hospital Discharge by CPR Duration Stratified by Patient Illness Category (Adjusted for initial pulseless rhythm, age category, weekend, night, extracorporeal membrane oxygenation, calcium administration, sepsis, renal insufficiency, vasoactive infusion during arrest, event location, sodium bicarbonate administration, prior history of a cardiopulmonary arrest, pre-arrest apnea monitor, pre-arrest pulse oximeter, and patient hypotension prior to arrest).

SUPPLEMENTAL FIGURE III. Proportion of (a) all patients with survival to hospital discharge, (b) survivors with favorable neurologic outcome, and (c) all patients with favorable neurologic outcome according to patient illness category and CPR duration, unadjusted. ***** $p<0.001$ compared to Trauma group; **†** $p<0.001$ compared to General Medical group; **‡** $p<0.01$ compared to Trauma; **§** $p<0.01$ compared to General Medical; **||** $p<0.05$ compared to Trauma; **#** $p<0.05$ compared to General Medical.

APPENDIX:

Get With The Guidelines-Resuscitation Investigators:

Besides the authors Robert Berg, MD and Vinay Nadkarni, MD, members of the GWTG-R Clinical Working Group/NRCPR Science Advisory Board and Pediatric Task Force include:

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