A tertiary care center’s experience with therapeutic hypothermia after pediatric cardiac arrest*

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**Objective:** To describe the use and feasibility of therapeutic hypothermia after pediatric cardiac arrest.

**Design:** Retrospective cohort study.

**Setting:** Pediatric tertiary care university hospital.

**Patients:** Infants and children (age 1 wk to 21 yrs) without complex congenital heart disease with return of spontaneous circulation after in-hospital or out-of-hospital cardiac arrest from 2000 to 2006.

**Intervention:** None.

**Measurements and Main Results:** We studied 181 patients after cardiac arrest, of which 91% were asphyxial in etiology (vs. cardiac) and 52% occurred in-hospital. Overall survival to hospital discharge was 45%. Forty patients received therapeutic hypothermia; all were admitted during or after 2002. Sixty percent of patients in the therapeutic hypothermia group had an initial temperature <35°C. The median therapeutic hypothermia target temperature was 34.0°C (33.5–34.8°C), was reached by 7 hrs (5–8 hrs) after admission in patients who were not hypothermic on admission, and was maintained for 24 hrs (16–48 hrs). Rewarming lasted 6 hrs (5–8 hrs). In the therapeutic hypothermia group, temperature <32°C occurred in 15% of patients and was associated with higher hospital mortality (29% vs. 11%; p = .02). Patients treated with therapeutic hypothermia differed from those treated with standard therapy, with more un-witnessed cardiac arrest (p = .04), more doses of epinephrine to achieve return of spontaneous circulation (p = .03), and a trend toward more out-of-hospital cardiac arrests (p = .11). After arrest, therapeutic hypothermia patients received more frequent electrolyte supplementation (p < .05). Standard therapy patients were twice as likely as therapeutic hypothermia patients to have a fever (>38°C) after arrest (37% vs. 18%; p = .02) and trended toward a higher rate of re-arrest (26% vs. 13%; p = .09). Rates of red blood cell transfusions, infection, and arrhythmias were similar between groups. There was no difference in hospital mortality (55.0% therapeutic hypothermia vs. 55.3% standard therapy; p = 1.0), and 78% of the therapeutic hypothermia survivors were discharged home (vs. 68% of the standard therapy survivors; p = .46). In multivariate analysis, mortality was independently associated with initial hypoglycemia or hyperglycemia, number of doses of epinephrine during resuscitation, asphyxial etiology, and longer duration of cardiopulmonary resuscitation, but not treatment group (odds ratio for mortality in the therapeutic hypothermia group, 0.47; p = .2).

**Conclusions:** This is the largest study reported on the use of therapeutic mild hypothermia in pediatric cardiac arrest to date. We found that therapeutic hypothermia was feasible, with target temperature achieved in <3 hrs overall. Temperature below target range was associated with increased mortality. Prospective study is urgently needed to determine the efficacy of therapeutic hypothermia in pediatric patients after cardiac arrest. (Pediatr Crit Care Med 2010; 11:66–74)

**Key Words:** brain injury; cardiopulmonary resuscitation; cardiac arrest; pediatric; outcome

*See also p. 151.

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Although cardiac arrest (CA) in infants and children in North America is uncommon, outcomes are dismal. Survival to hospital discharge after out-of-hospital CA is 2% to 28% and is 14% to 42% after in-hospital CA. Many survivors have severe neurologic disability (1–8).

In experimental models of cerebral ischemia-reperfusion injury and CA, hypothermia (HT) mitigated alterations in the cellular environment, namely excitotoxicity, calcium flux, cell signaling, inflammation, free radical and edema formation, apoptosis, and necrosis (9–13). Randomized controlled trials have shown mild (32°C–34°C) HT to be effective in improving neurologic outcome after arrhythmia-induced adult CA and birth asphyxia (14–17). Despite potential complications of HT (e.g., arrhythmias, coagulopathy, and infection), there was no increase in adverse events compared to normothermic control patients (18,19).

No therapy has been shown to improve outcome for pediatric patients after CA, in which the primary etiology is asphyxia (4). Asphyxia is associated with poorer outcomes than arrhythmia-induced CA and has a distinct pathophysiology (20, 21). Nearly 30 yrs ago, Conn et al (22) proposed HYPER therapy as a cerebral resuscitation strategy after return of spontaneous circulation (ROSC) for drowned children, which included mod-
erate HT (30°C), diuretics, hyperventilation (Paco₂ 30 torr), steroids, phenobarbital (target serum level 50–75 mg/L), neuromuscular blockade, intracranial pressure monitoring, and intracranial pressure-directed therapy. This regimen excluding steroids was retrospectively shown to be associated with neutropenia and increased risk of bacteremia without improving outcome, leading to discontinuation of HT and intracranial pressure-directed therapy in these patients (23). Contemporary models of global asphyxial CA in prepubertal and adult animals have demonstrated robust neurologic benefits using mild HT, but clinical studies are lacking (13, 24–27). Specifically, studies are needed evaluating the feasibility, safety, and efficacy of mild HT in children, and the National Institutes of Health is supporting a multicenter, randomized, controlled trials investigating therapeutic HT after pediatric CA, which began enrolling subjects in September 2009 later last year (personal communication, Frank Moler, MD, MS; 28).

In 2002, after the publication of two adult HT randomized, controlled trials (14, 15), pediatric critical care physicians at our institution began cooling selected patients who were comatose after CA. Here, we describe our center’s experience with the use of HT in children surviving CA.

MATERIALS AND METHODS

Design and Setting

This study was approved by the University of Pittsburgh Institutional Review Board. We performed a retrospective chart review of patients who had in-hospital or out-of-hospital CA between July 1, 2000 and August 31, 2006, and were admitted to the pediatric intensive care unit (ICU) at the Children’s Hospital of Pittsburgh. Children’s Hospital of Pittsburgh is a tertiary care and level I trauma center with 13,000 admissions per year. The multidisciplinary pediatric ICU has approximately 2400 admissions per year. The cardiac ICU is a separate unit, and the hospital does not have a burn unit. HT was used at the discretion of the attending physician. We had no protocol for its use.

Inclusion and Exclusion Criteria

We studied infants and children 1 wk to 21 yrs of age admitted to the ICU with ROSC after CA. CA was defined as receipt of chest compressions for pulselessness as determined by a health care worker. We excluded children with congenital heart disease. Subjects were identified by searching the ICU quality-assurance database for an International Classification of Diseases-9 discharge diagnosis of CA (427.5) (29). For patients with multiple CA during the hospitalization, information surrounding the first arrest was used for Utstein-style data collection, and the occurrence of re-arrest was recorded (30). Some patients were dependent on mechanical ventilation before their CA (n = 11), and others became dependent after CA (n = 10).

Data Collection

Etiology of CA was determined by medical record review. When available, we abstracted the duration of time from the beginning of a witnessed CA and the beginning of resuscitation until ROSC, the occurrence of seizures (detected clinically or on electroencephalogram) in the first 4 days after CA, and the number of intropes and vasoressors (i.e., epinephrine, norepinephrine, vasopressin, milrinone, dopamine, dobutamine) initiated in the first 24 hrs after CA. Temperature, heart rate, and mean arterial blood pressure were documented hourly for clinical care of all ICU patients, but only abstracted for the HT group. We normalized heart rate and mean arterial blood pressure for age and gender (31, 32). Rectal temperatures were measured on most patients, but method of temperature measurement was not uniform.

Definitions

Cardiac rhythm monitoring was not always performed during the period of pulselessness. Therefore, the first monitored rhythm was the first rhythm recorded either during or after the CA. A non-chronic illness was defined as an acute, new medical problem, and chronic illness was defined as a long-standing or recurrent medical problem. We used the National Institute of Diabetes and Digestive and Kidney Diseases definition of hypoglycemia <70 mg/dL and defined hyperglycemia as >250 mg/dL, which is associated with increased mortality in critically ill patients (33). Immunosuppressed patients had cancer, primary immune deficiency, or underwent a solid organ or bone marrow transplantation.

Care After Resuscitation

Although Children’s Hospital of Pittsburgh did not have a protocol for care after resuscitation, there were general standards of care. Patients who remained comatose after ROSC received central venous and arterial catheters. Anti-epileptic medications were started only if the patient also incurred a traumatic brain injury or had a clinical or electrographic seizure. Pain and sedation medications were used at the discretion of the attending physician and were often withheld initially to obtain a neurologic examination. There was no protocol regarding therapy for hyperglycemia in non-diabetic patients; however, practice by ICU attendings may have changed after the publication of a study showing reduced mortality in surgical intensive care adult patients (34). Total parental nutrition was typically instituted by 48 hrs. Enteral feeding was initiated as soon as feasible. We did not routinely obtain electroencephalograms or blood cultures.

Cooling Methods

In patients with severe trauma, hospital policy early in the study period mandated active warming to normothermia in the emergency department (n = 11 standard therapy [ST] patients) with warm lights, intravenous fluids, and bedding. In all other cases, the

![Figure 1. Study flowchart. Hypothermia (HT) data are presented as mean ± SD and median (interquartile range). ROSC, return of spontaneous circulation; h, hour; n, number.](Image)
attending ICU physician decided whether to initiate HT treatment and determined the target temperature, duration, and rate of re-warming. Most ST patients without severe trauma were passively warmed to normothermia.

Induction of HT was accomplished with multiple modalities. Most commonly, we used a cooling blanket (Cincinnati SubZero Plastipad, Cincinnati, OH) positioned under the patient and controlled by an automated cooling system (Gaymar Medi-Therm III, Orchard Park, NY) set to the target temperature. Other methods included surface cooling with ice packets, bath and fan, lowering of the room and ventilator humidifier thermostat, and, occasionally, gastric lavage with iced saline. One patient received 40 mL/kg of intravenous iced saline to induce HT. Nondepolarizing neuromuscular blockers were often used to prevent shivering during induction of HT. Fever (>38°C) was treated aggressively in all patients with methods similar to those used for cooling induction, as well as with anti-pyretics (e.g., acetaminophen). Authors have defined fever as any temperature above normal (>38°C or 38.5°C) (35–37). In our ICU, temperatures >38°C provoke a search for an etiology and an effort to actively reduce the temperature because of the risk of higher temperatures and resultant secondary brain injury (38). Re-warming was achieved by increasing the set point of the cooling blanket gradually until the patient reached 36°C, at which time the blanket was turned off to prevent over-warming.

Outcome Measures

The primary outcomes were logistics related to the application of HT and the frequency of adverse events in the first 4 days after CA. Adverse events included hemorrhage, transfusion, positive cultures, electrolyte supplementation, intermittent arrhythmia (any abnormal rhythm documented in the chart that did not precipitate a re-arrest), and re-arrest. The number of red blood cell transfusions was obtained from the hospital’s blood bank. Positive cultures were defined as any culture positive for bacteria, virus, or fungus from tracheal, blood, cerebrospinal fluid, or urine. A positive tracheal culture was defined as bacterial growth from a tracheal sample which time the blanket was turned off to prevent over-warming.

Secondary outcomes included mortality and Glasgow Outcome Score (GOS) (assigned in a non-blinded fashion based on medical records for both pre-arrest and hospital discharge status), a variation on the Utstein recommendation (30). GOS categories are defined as: (1) dead; (2) persistent vegetative or minimally conscious state; (3) moderate disability; (4) mild disability; and (5) no disability.

Data Analysis

The data were analyzed for treatment group differences with Fisher’s exact tests for categorical variables and Student’s t tests for normally distributed continuous variables. Wilcoxon rank-sum was used for non-normally distributed data. Associations with outcomes between patients in the HT or ST group were determined by univariate analysis. Variables with p < .1 for mortality were included in a multivariable logistic regression model using a backward stepwise method, and variables with the highest p values were eliminated sequentially until all terms in the model were significant (p < .05). HT was forced into the final model, although its p value was > .1. Initial variables in the multivariable re-

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total, n = 181</th>
<th>ST, n = 141</th>
<th>HT, n = 40</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in yrs</td>
<td>60 ± 6.2</td>
<td>60 ± 6.2</td>
<td>60 ± 6.6</td>
<td>.8</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.9 (0.7–11.2)</td>
<td>2.9 (1.1–11.1)</td>
<td>2.4 (4–11.8)</td>
<td>.9</td>
</tr>
<tr>
<td>Gender, male/female (% male)</td>
<td>104/77 (57.5)</td>
<td>80/61 (56.7)</td>
<td>24/16 (60.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>126 (70.0)</td>
<td>97 (69.3)</td>
<td>29 (72.5)</td>
<td>.7</td>
</tr>
<tr>
<td>Black</td>
<td>29 (16.1)</td>
<td>23 (16.4)</td>
<td>6 (15.0)</td>
<td>.6</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>25 (13.9)</td>
<td>20 (14.3)</td>
<td>5 (12.5)</td>
<td>.6</td>
</tr>
<tr>
<td>Insurance status, n (%)b</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>111 (62.7)</td>
<td>87 (63.5)</td>
<td>24 (60.0)</td>
<td>.1</td>
</tr>
<tr>
<td>Private</td>
<td>58 (32.8)</td>
<td>43 (31.4)</td>
<td>15 (37.5)</td>
<td></td>
</tr>
<tr>
<td>Self-pay</td>
<td>8 (4.52)</td>
<td>7 (5.1)</td>
<td>1 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Pre-existing illness, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>55 (35.7)</td>
<td>43 (35.2)</td>
<td>12 (37.5)</td>
<td>.7</td>
</tr>
<tr>
<td>Not chronic</td>
<td>35 (22.7)</td>
<td>26 (21.3)</td>
<td>9 (28.1)</td>
<td></td>
</tr>
<tr>
<td>Chronic</td>
<td>64 (41.6)</td>
<td>53 (43.4)</td>
<td>11 (34.3)</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressed, n (%)</td>
<td>17 (9.4)</td>
<td>16 (11.3)</td>
<td>1 (2.5)</td>
<td>.1</td>
</tr>
</tbody>
</table>

ST, standard therapy; HT, hypothermia therapy; IQR, interquartile range.

a ST vs. HT; b numbers of subjects for race/ethnicity, insurance status, and pre-existing illness do not equal column totals because of missing data. Race/ethnicity data were available for 180, insurance data for 177, and pre-existing illness for 154 subjects.

Table 2. Etiology of cardiac arrest

<table>
<thead>
<tr>
<th>Etiologyb</th>
<th>Total, n = 180</th>
<th>All ST, n = 140</th>
<th>ST After 2001, n = 95</th>
<th>HT, n = 40</th>
<th>p*</th>
<th>Mortality by Etiology, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary disease,c n (%)</td>
<td>43 (23.8)</td>
<td>36 (25.5)</td>
<td>28 (29.5)</td>
<td>7 (17.5)</td>
<td>.8</td>
<td>42</td>
</tr>
<tr>
<td>Trauma</td>
<td>23 (12.7)</td>
<td>21 (14.9)</td>
<td>16 (16.8)</td>
<td>2 (5.0)</td>
<td>.9</td>
<td>70</td>
</tr>
<tr>
<td>Sepsis or septic shock</td>
<td>22 (12.2)</td>
<td>18 (12.8)</td>
<td>14 (14.7)</td>
<td>4 (10.0)</td>
<td>.6</td>
<td>64</td>
</tr>
<tr>
<td>SIDS</td>
<td>17 (9.4)</td>
<td>11 (7.8)</td>
<td>5 (5.3)</td>
<td>6 (15.0)</td>
<td>.08</td>
<td>76</td>
</tr>
<tr>
<td>Submersion</td>
<td>15 (8.3)</td>
<td>8 (5.7)</td>
<td>4 (4.2)</td>
<td>7 (17.5)</td>
<td>.02</td>
<td>40</td>
</tr>
<tr>
<td>Cardiacc</td>
<td>14 (7.7)</td>
<td>9 (6.4)</td>
<td>5 (5.3)</td>
<td>5 (12.5)</td>
<td>.05</td>
<td>29</td>
</tr>
<tr>
<td>Hemorrhage, non-trauma</td>
<td>10 (5.5)</td>
<td>6 (4.3)</td>
<td>4 (4.2)</td>
<td>4 (10.0)</td>
<td>.08</td>
<td>60</td>
</tr>
<tr>
<td>Inflicted TBI</td>
<td>9 (5.0)</td>
<td>8 (5.7)</td>
<td>5 (5.3)</td>
<td>1 (2.5)</td>
<td>1.0</td>
<td>78</td>
</tr>
<tr>
<td>Neurologic disease, non-trauma</td>
<td>9 (5.0)</td>
<td>8 (5.7)</td>
<td>5 (5.3)</td>
<td>1 (2.5)</td>
<td>1.0</td>
<td>78</td>
</tr>
<tr>
<td>Status epileptic</td>
<td>7 (3.9)</td>
<td>5 (3.5)</td>
<td>1 (1.1)</td>
<td>2 (5.0)</td>
<td>.1</td>
<td>71</td>
</tr>
<tr>
<td>Abdominal catastrophe</td>
<td>4 (2.2)</td>
<td>3 (2.1)</td>
<td>3 (3.2)</td>
<td>1 (2.5)</td>
<td>1.0</td>
<td>75</td>
</tr>
<tr>
<td>Abnormal electrolytes</td>
<td>3 (1.7)</td>
<td>3 (2.1)</td>
<td>2 (2.1)</td>
<td>0 (0.0)</td>
<td>1.0</td>
<td>33</td>
</tr>
<tr>
<td>Toxic ingestion</td>
<td>1 (0.6)</td>
<td>1 (0.7)</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>1.0</td>
<td>33</td>
</tr>
<tr>
<td>Other</td>
<td>3 (1.7)</td>
<td>3 (2.1)</td>
<td>2 (2.1)</td>
<td>0 (0.0)</td>
<td>1.0</td>
<td>33</td>
</tr>
</tbody>
</table>

ST, standard therapy; HT, hypothermia therapy; SIDS, sudden infant death syndrome; TBI, traumatic brain injury.

*Etiologies were available for 180 of the 181 study patients (and 140 of the 141 ST patients); b etiologies are mutually exclusive; c ST vs. HT, all patients 2002 to 2006 only; d includes asthma, pulmonary infections, and aspiration; e includes cardiomyopathy, arrhythmia, and heart transplant recipients for cardiomyopathy.
gression included first whole blood pH, initial glucose (<70 mg/dL, 70–250 mg/dL, >250 mg/dL), epinephrine doses during resuscitation (0, 1–3, or ≥6), number of inotropes in the first 24 hrs, location of CA (out-of-hospital vs. in-hospital), etiology of CA (asphyxia vs. cardiac), whether the arrest was witnessed, HT vs. ST, and minutes of cardiopulmonary resuscitation until ROSC. All p values were two-sided. Missing data were not imputed. Data are presented as median (interquartile range [IQR]) or mean ± sd. Data analysis was performed using Stata software, version 10 (College Station, TX).

RESULTS

In the 6-yr study period, 399 children had the discharge diagnosis CA, 181 of whom met entry criteria and were included in this study (Fig. 1). Forty subjects received HT. Baseline patient characteristics were similar between HT and ST groups (Table 1), with the exception that more immuno-suppressed patients were in the ST group (p = .1). Only one-third of children had no chronic illnesses.

Details of CA, Resuscitation, and Management After Resuscitation

Ninety percent of children with CA had asphyxia as the cause of their CA, and 55% of CA occurred in-hospital (Tables 2 and 3). Important differences existed between HT and ST groups with regard to duration of cardiopulmonary resuscitation to ROSC, doses of epinephrine during resuscitation, and witnessed arrest status.

Logistics of Hypothermia Treatment

All 40 children receiving HT were admitted during or after 2002. The median temperature on presentation to the ICU was lower in the HT vs. ST group (34.2°C [32.3°C–35.3°C] vs. 35.4°C [33.6°C–36.3°C]; p < .01). The majority (60%) of children in the HT group presented to the ICU with temperatures at or below the target temperature and therefore required only maintenance cooling. Temperature <36°C or >38°C on arrival to the ICU was associated with increased mortality (vs. 36°C–38°C; p < .01). The median HT target temperature was 34.0°C (33.5°C–34.8°C), was reached by 7 hrs (5–8 hrs) in patients who had temperature above target on admission, and was maintained for 24 hrs (16–48 hrs). A cooling blanket was used for 84% of HT patients. Re-warming lasted 6 hrs (5–8 hrs). Eleven children, six with trauma before 2002, were actively warmed to normothermia. Three of these patients progressed to brain death, one died without brain death, and seven survived.

Table 3. Details of cardiac arrest, resuscitation, treatment, and outcome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total, n = 181</th>
<th>ST, n = 141</th>
<th>HT, n = 40</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary etiology, n (%)</td>
<td>164 (91.1)</td>
<td>129 (92.1)</td>
<td>35 (87.5)</td>
<td>.4</td>
</tr>
<tr>
<td>Asphyxia</td>
<td>16 (8.9)</td>
<td>11 (7.9)</td>
<td>5 (12.5)</td>
<td>.11</td>
</tr>
<tr>
<td>Location, n (%)</td>
<td>94 (54.9)</td>
<td>78 (55.3)</td>
<td>16 (40.0)</td>
<td>.11</td>
</tr>
<tr>
<td>In-hospital</td>
<td>87 (45.1)</td>
<td>63 (44.7)</td>
<td>24 (60.0)</td>
<td>.11</td>
</tr>
<tr>
<td>Out-of-hospital</td>
<td>136 (75.6)</td>
<td>111 (79.3)</td>
<td>25 (62.5)</td>
<td>.04</td>
</tr>
<tr>
<td>Witnessed, n (%)</td>
<td>14.5 ± 14.5</td>
<td>13.5 ± 14.8</td>
<td>18.2 ± 13.0</td>
<td>.02</td>
</tr>
<tr>
<td>Interval of CA to ROSC, min</td>
<td>10 (4–20)</td>
<td>8 (3–15)</td>
<td>15 (10–26)</td>
<td>.06</td>
</tr>
<tr>
<td>Interval of CPR to ROSC, minutes</td>
<td>15 ± 14.4</td>
<td>14.5 ± 14.8</td>
<td>17.4 ± 12.6</td>
<td>.04</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>10 (5–20)</td>
<td>9 (4–20)</td>
<td>15 (8–26)</td>
<td>.06</td>
</tr>
<tr>
<td>First monitored rhythm, n (%)</td>
<td>90% of children with CA</td>
<td>97% of children with CA</td>
<td>97% of children with CA</td>
<td>.03</td>
</tr>
<tr>
<td>Epinephrine doses</td>
<td>2 ± 2.5</td>
<td>2 ± 2.3</td>
<td>3 ± 3.0</td>
<td>.03</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>2 (0–3)</td>
<td>1.5 (0–3)</td>
<td>2 (1–4)</td>
<td>.03</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>11 (6.1)</td>
<td>6 (4.3)</td>
<td>5 (12.5)</td>
<td>.07</td>
</tr>
<tr>
<td>Initial glucose, mg/dL, mean ± sd</td>
<td>224 ± 123</td>
<td>224 ± 129</td>
<td>223 ± 98</td>
<td>1.0</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>8.5 ± 6.9</td>
<td>8.5 ± 7.2</td>
<td>8.5 ± 6.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Temperature on ICU admission, °C</td>
<td>34.6 ± 2.2</td>
<td>34.8 ± 2.1</td>
<td>33.9 ± 2.2</td>
<td>.02</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>35.1 (33.3–36.1)</td>
<td>35.4 (33.6–36.3)</td>
<td>34.2 (32.3–35.3)</td>
<td>.04</td>
</tr>
<tr>
<td>Number of inotropes during first 24 hrs</td>
<td>1.5 ± 1.4</td>
<td>1.5 ± 1.4</td>
<td>1.7 ± 1.4</td>
<td>.04</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>1 (0–3)</td>
<td>1 (0–3)</td>
<td>2 (1–5)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>58 (32.2)</td>
<td>35 (25.0)</td>
<td>23 (37.5)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Insulin infusion during first 24 hrs, n (%)</td>
<td>67 (37.2)</td>
<td>52 (37.1)</td>
<td>15 (37.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hydrocortisone infusion during first 24 hrs, n (%)</td>
<td>50 (27.8)</td>
<td>28 (20.0)</td>
<td>22 (55.0)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Neur muscular blockade during first 24 hrs, n (%)</td>
<td>15.7 ± 33.2</td>
<td>14.9 ± 28.4</td>
<td>18.4 ± 46.8</td>
<td>.04</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>4 (2–13)</td>
<td>4 (1–13)</td>
<td>7 (3–13)</td>
<td>.5</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>39.9 (33.4–45.4)</td>
<td>29.6 (23.5–36.0)</td>
<td>51.1 (40.3–59.9)</td>
<td>.5</td>
</tr>
<tr>
<td>Duration of artificial airway, days</td>
<td>20.1 ± 38.7</td>
<td>20.1 ± 35.9</td>
<td>20.0 ± 47.7</td>
<td>.04</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>6 (1–19)</td>
<td>5 (1–24)</td>
<td>7 (2–18)</td>
<td>.5</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>25.6 ± 43.6</td>
<td>25.0 ± 40.7</td>
<td>27.4 ± 53.2</td>
<td>.5</td>
</tr>
<tr>
<td>Hospital length of stay, days</td>
<td>8 (2–32)</td>
<td>8 (2–32)</td>
<td>9 (3–25)</td>
<td>.5</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>32 (17.7)</td>
<td>24 (17.0)</td>
<td>8 (20.0)</td>
<td>.6</td>
</tr>
<tr>
<td>Seizures during first 4 days, n (%)</td>
<td>4.5 ± 0.8</td>
<td>4.5 ± 0.8</td>
<td>4.7 ± 0.6</td>
<td>.5</td>
</tr>
<tr>
<td>Pre-CA GOS, mean ± sd</td>
<td>2.4 ± 1.6</td>
<td>2.4 ± 1.6</td>
<td>2.4 ± 1.7</td>
<td>.9</td>
</tr>
<tr>
<td>Hospital discharge GOS, mean ± sd</td>
<td>100 (55.2)</td>
<td>78 (55.3)</td>
<td>22 (55.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Mortality, n (%)</td>
<td>64 (35.4)</td>
<td>51 (36.2)</td>
<td>13 (32.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>Withdrawal of technological support, n (%)</td>
<td>10 (5.5)</td>
<td>7 (5.0)</td>
<td>3 (7.5)</td>
<td>.7</td>
</tr>
</tbody>
</table>

CA, CA, cardiac arrest; ROSC, return of spontaneous circulation; IQR, interquartile range; ICU, intensive care unit; ST, standard therapy; HT, hypothermia therapy; GOS, Glasgow Outcome Scale; CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; VT, ventricular tachycardia; VF, ventricular fibrillation; NSR, normal sinus rhythm; V-A ECMO, venous-arterial extracorporeal mechanical oxygenation.

*ST vs. HT; **N = 126 total, 101 ST, and 25 HT patients. Time from pulselessness to ROSC; **N = 138 total, 111 ST, and 27 HT patients. Time from initiation of CPR to ROSC; ***N = 152 total, 119 ST, and 33 HT patients.
Table 4. Adverse events in the first 4 days

<table>
<thead>
<tr>
<th>Type of Event</th>
<th>Total, n = 181</th>
<th>ST, n = 141</th>
<th>HT, n = 40</th>
<th>( p^a )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmias, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermittent</td>
<td>9 (6.0)</td>
<td>6 (4.3)</td>
<td>3 (7.5)</td>
<td>.4</td>
</tr>
<tr>
<td>Re-arrest</td>
<td>41 (22.7)</td>
<td>36 (25.5)</td>
<td>5 (12.5)</td>
<td>.09</td>
</tr>
<tr>
<td>Positive culture, n (%)</td>
<td>97 (53.6)</td>
<td>73 (51.8)</td>
<td>24 (60.0)</td>
<td>.17</td>
</tr>
<tr>
<td>Days 1 and 2</td>
<td>81 (44.8)</td>
<td>62 (44.3)</td>
<td>19 (47.5)</td>
<td>.3</td>
</tr>
<tr>
<td>Tracheal aspirate</td>
<td>50 (27.6)</td>
<td>34 (24.4)</td>
<td>16 (40.0)</td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>17</td>
<td>15</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Viral</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Days 3 and 4</td>
<td>16 (8.8)</td>
<td>11 (7.9)</td>
<td>5 (12.5)</td>
<td>.2</td>
</tr>
<tr>
<td>Tracheal aspirate</td>
<td>8</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Viral</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Number of RBC transfusions,</td>
<td></td>
<td></td>
<td></td>
<td>.15</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>3.8 (7.7)</td>
<td>3.7 (8.4)</td>
<td>4.2 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>2 (1–4)</td>
<td>2 (1–3)</td>
<td>2 (1–7)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage, n (%)</td>
<td>8 (4.4)</td>
<td>7 (5.0)</td>
<td>1 (25.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Doses of electrolytes, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>85 (47.0)</td>
<td>78 (55.3)</td>
<td>7 (17.5)</td>
<td></td>
</tr>
<tr>
<td>1–3 doses</td>
<td>40 (22.1)</td>
<td>31 (22.0)</td>
<td>9 (22.5)</td>
<td></td>
</tr>
<tr>
<td>≥4 doses</td>
<td>56 (30.9)</td>
<td>32 (22.7)</td>
<td>24 (60.0)</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.01</td>
</tr>
<tr>
<td>0 doses</td>
<td>134 (74.0)</td>
<td>111 (78.1)</td>
<td>23 (57.5)</td>
<td></td>
</tr>
<tr>
<td>1–3 doses</td>
<td>42 (23.2)</td>
<td>29 (20.6)</td>
<td>13 (30.5)</td>
<td></td>
</tr>
<tr>
<td>≥4 doses</td>
<td>5 (2.8)</td>
<td>1 (1.7)</td>
<td>4 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td></td>
<td></td>
<td></td>
<td>.08</td>
</tr>
<tr>
<td>0 doses</td>
<td>161 (89.0)</td>
<td>129 (91.5)</td>
<td>32 (80.0)</td>
<td></td>
</tr>
<tr>
<td>1–3 doses</td>
<td>16 (8.8)</td>
<td>9 (6.4)</td>
<td>7 (17.5)</td>
<td></td>
</tr>
<tr>
<td>≥4 doses</td>
<td>4 (2.2)</td>
<td>3 (2.1)</td>
<td>1 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Phosphorus</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.01</td>
</tr>
<tr>
<td>0 doses</td>
<td>140 (77.3)</td>
<td>117 (83.0)</td>
<td>23 (57.5)</td>
<td></td>
</tr>
<tr>
<td>1–3 doses</td>
<td>39 (21.6)</td>
<td>22 (15.6)</td>
<td>17 (42.5)</td>
<td></td>
</tr>
<tr>
<td>≥4 doses</td>
<td>2 (1.1)</td>
<td>2 (1.4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Fever, n (%)</td>
<td>59 (33%)</td>
<td>52 (37%)</td>
<td>7 (18%)</td>
<td>.02</td>
</tr>
<tr>
<td>Temperature below target, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>&lt;32°C</td>
<td>6 (15.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;31°C</td>
<td>5 (12.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30°C</td>
<td>4 (10.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RBC, red blood cells; ST, standard therapy; HT, hypothermia; IQR, interquartile range.

*aST vs. HT; b bacterial infection, unless noted otherwise; c positive cultures with the same organism and site for a patient were counted once; d patient with gunshot wound to head; e patient on extracorporeal membrane oxygenation (ECMO); f two patients with liver failure/short gut syndrome, one patient with multi-system trauma, one patient with sepsis after multi-visceral transplantation; g patient with postoperative coagulopathy and gastrointestinal hemorrhage; h patient on ECMO; i fever was defined as ≥38°C; \( p \) value is comparing hospital mortality among HT patients with temperature ≥32°C vs. ≤32°C.

Safety

The HT and ST groups had similar rates of hemorrhage, receipt of red blood cell transfusions, intermittent arrhythmias, infection, and seizures in the first 4 days of admission (Table 4).

Three children had bradycardia (<60 beats per minute) for >1 hr (range, 2–11 hrs) during HT (Figs. 2A, B, C). All were older than 12 yrs, with corresponding normal to high blood pressures, and all had a GOS of 5 (normal) on hospital discharge. Mean arterial blood pressure did not change significantly on re-warming in the HT group, but heart rate increased after re-warming.

Patients in the HT group received more frequent potassium, magnesium, and phosphorus supplementation than those in the ST group (\( p < .05 \)) and trended toward more calcium supplementation (\( p = .08 \)). Patients in the HT group also received more insulin infusions in the first 4 days, both for the entire study period (\( p < .01 \)) and for patients admitted in or after 2002 (\( p = .02 \)).

Patients in the HT group with temperature <32°C had increased hospital mortality compared with patients whose temperature remained ≥32°C (73% vs. 43%; \( p = .02 \)), even excluding patients with admission temperature <30°C (\( p = .03 \)). However, there was a trend toward fewer re-arrests in children treated with HT vs. ST (5 [13%] vs. 36 [26%]; \( p = .09 \)).

Fever (>38°C) in the first 4 days occurred more frequently in the ST group vs. the HT group (38% vs. 18%; \( p = .02 \)). Three children in the HT group had fever in the first 24 hrs on re-warming. Neither mortality nor GOS was associated with fever in the first 4 days.

Outcomes

Mortality was similar between groups (55.0% HT vs. 55.3% ST; \( p = 1.0 \)). Mortality did not improve over time and ranged from 34% to 70% per year. Extracorporeal membrane oxygenation (ECMO) was not associated with mortality overall (5 of 11 [45%] ECMO patients died vs. 95 of 170 [56%] non-ECMO; \( p = .54 \)) or within each group (HT mortality: 40% ECMO vs. 57% non-ECMO; \( p = .6 \); ST mortality: 50% ECMO vs. 56% non-ECMO; \( p = 1.0 \)). However, mortality was only 27% in children who had ROSC after cardiopulmonary resuscitation without epinephrine (\( n = 48 \) vs. 65% in children requiring at least one dose of epinephrine to achieve ROSC (\( n = 133 \)). In bivariate and multivariate analysis, HT was not associated with survival. (Table 5).

Discussion

To our knowledge, this is the largest study reporting on the use of HT after pediatric CA. We found that mild HT in children after ROSC is feasible using resources readily available in this tertiary pediatric ICU. However, we also identified important safety issues related to cooling below target temperature and depletion of electrolytes.

HT for neuroprotection after CA from asphyxia has been studied prospectively only in neonates, but inpatient adults treated with HT after pulseless electrical activity or asystole demonstrated a trend toward better outcome in an observational study (18). Current American
Heart Association guidelines recommend the use of HT for adults remaining comatose after CA from ventricular arrhythmia and the consideration of HT for comatose survivors of pediatric CA (39).

Time to target temperature in our patients was comparable to that reported in adult and neonatal randomized, controlled trials, although the median target temperature in this cohort was higher (34°C vs. 32°C–34°C) (14, 15, 17), and almost half of the children who attained ROSC had an initial temperature <35°C. The higher target temperatures may reflect inexperience with the use of HT, lack of evidence of benefit in pediatric patients after CA, or caution in patients thought to be at higher risk for adverse effects from HT (e.g., patients with trauma or arrhythmia). Similar to other studies of children with acute brain injury, abnormal temperature on presentation to the ICU was associated with increased mortality (40–48). Temperature below target range in the HT group occurred less frequently (15%) than in an adult cohort (63%) (49), suggesting that temperature may be easier to control in children. It is not clear, however, if presence of a poikilothermic state is reflective of severe injury and thus an increased risk of death, and/or if temperature below target range itself causes an increase in mortality.

We were surprised that 38% of children in the ST group had fever in the first 4 days after CA. Given the well-documented detrimental effects of fever in animal models of brain ischemia, this could represent an important target for improvement by health care providers and cooling technologies. Since 2002, our trauma protocol has been modified to discontinue active warming of children with brain injury (38).

Patients in the HT group tended to be treated with ECMO more frequently, but ECMO was not associated with a higher or lower mortality risk. Children with congenital heart disease, who were excluded from this study, have benefitted the most from ECMO cardiopulmonary resuscitation (50, 51). The use of neuromuscular blockade was greater in the HT group, to provide more precise patient temperature control, to prevent shivering, and to promote ventilator synchrony. The greater number of days with an artificial airway in patients treated with HT may be a consequence of the intervention itself (patients remained intubated until re-warming was completed).

Despite similar initial serum glucose concentration after ROSC, insulin infusions were used twice as frequently in the HT group, which may be a reflection of HT-related hyperglycemia. As in patients with traumatic brain injury and congenital heart surgery, hyperglycemia was associated with increased mortality (52–56). Hypoglycemia on ICU presentation was also associated with increased mortality, perhaps reflecting a poor stress response or long-standing nutrient deprivation causing cellular energy depletion. Hypoglycemia induces neuronal cell death in the same vulnerable areas as does hypoxia-ischemia (the CA1 hip-
pocampus, cerebral cortex, basal ganglia, and thalamus), and likely exacerbates neuronal cell death after CA (57). Optimal glucose management after CA in children is unknown and may be a critical element in management after resuscitation.

As in the adult and neonatal randomized, controlled trials, HT was not associated with increased arrhythmias, severe bleeding events, or red cell transfusions (14–17). We also found no difference in the incidence of seizures or positive cultures. Groups had similar rates of sepsis or septic shock as the etiology of CA.

Patients in the HT group received more electrolyte supplementation. Although this finding is similar to adult traumatic brain injury patients treated with HT (who are at particular risk for low levels of phosphorus and magnesium), it has not been previously reported in the CA literature (58–61). Potential mechanisms mediating electrolyte depletion are: cold diuresis, which increases water and electrolyte losses and has greatest effect during active cooling; osmotic diuresis from hyperglycemia; increased insulin use in the HT group; and intracellular shifts of electrolytes during HT (58–61).

Hemodynamic changes can occur during HT and re-warming. Cardiac output decreases during HT secondary to decreased heart rate and decreased stroke volume and increased afterload from peripheral vasoconstriction. It typically increases back to baseline during re-warming (62, 63). Mean arterial blood pressure can decrease on re-warming, which can be partly explained by peripheral vasoconstriction and a relative hypovolemic state. This occurred in only one patient in our study, suggesting that care was taken to avoid this complication (64). Finally, the metabolism and effects of commonly used medications are influenced by systemic HT and may result in altered hemodynamics (65).

Patients in our study had higher survival rates than those in previous reports (3, 4), at least partially because we included only patients who survived to ICU admission. Also, we included all patients receiving cardiopulmonary resuscitation who had pulselessness documented by a health care worker, even if the event was brief (e.g., a plugged endotracheal tube in the ICU). One-third of the patients did not require bolus epinephrine for ROSC, and they had twice the survival rates of patients receiving epinephrine. Finally, large reviews of pediatric CA include data from hospitals that do not specialize in pediatric care.

Study Limitations

In this observational study, we were unable to fully adjust for the effects of selection bias or effects of temporal trends. We therefore cannot determine the efficacy of HT in children after CA. The purpose of the study was to describe our experience using HT and help care providers anticipate and prevent adverse events. Data collection was limited by available documentation. Children with congenital heart disease, a group with better outcome after CA, were excluded. GOS was assigned retrospectively in a non-blinded fashion using medical record entries. GOS is a gross measure of function and may not accurately depict outcome in infants. Our study does not include data on long-term outcomes or detailed cognitive function. Testing for infection and electrolyte levels was not standardized. There was no protocol for routine cultures in patients, and many children had cultures taken on the day of presentation with CA, whether signs and symptoms of sepsis were present, potentially biasing our data. Although electroencephalogram pattern has been associated with outcome after pediatric CA, we did not measure it in this study (66).

Rectal temperature probes are routinely used in our ICU, largely because they are simple to use. However, they may less accurately measure core temperature than other methods (67–72).

CONCLUSIONS

Pediatric patients with CA are in urgent need of proven interventions that improve outcome. Details regarding the optimal implementation of therapeutic HT in children after CA are needed. Common complications associated with HT may blunt its effectiveness, but that may be preventable. We believe that the efficacy of mild HT warrants prospective study in pediatric patients after CA.

ACKNOWLEDGMENTS

Special thanks to Suruchi Batra and Ronald Radocay for assistance in data ac-

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### Table 5. Univariate and multivariate analysis for mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>First whole blood pH</td>
<td>0.01</td>
<td>&lt;.01</td>
<td>0.00–0.10</td>
</tr>
<tr>
<td>Initial glucose 70–250 mg/dL</td>
<td>1</td>
<td>Reference group</td>
<td></td>
</tr>
<tr>
<td>Initial glucose &lt;70 mg/dL</td>
<td>3.36</td>
<td>.04</td>
<td>1.03–10.93</td>
</tr>
<tr>
<td>Initial glucose &gt;250 mg/dL</td>
<td>5.31</td>
<td>&lt;.01</td>
<td>2.67–10.53</td>
</tr>
<tr>
<td>No epinephrine bolus during resuscitation</td>
<td>1</td>
<td>Reference group</td>
<td></td>
</tr>
<tr>
<td>1–5 epinephrine doses</td>
<td>3.98</td>
<td>&lt;.01</td>
<td>1.96–8.09</td>
</tr>
<tr>
<td>≥6 epinephrine doses</td>
<td>28.8</td>
<td>&lt;.01</td>
<td>3.43–241.6</td>
</tr>
<tr>
<td>Number of inotropes first 24 hrs</td>
<td>1.48</td>
<td>&lt;.01</td>
<td>1.17–1.87</td>
</tr>
<tr>
<td>OOH (vs. IH) location of CA</td>
<td>2.48</td>
<td>&lt;.01</td>
<td>1.35–4.53</td>
</tr>
<tr>
<td>Cardiac (vs. asphyxia) etiology</td>
<td>0.16</td>
<td>&lt;.01</td>
<td>0.04–0.60</td>
</tr>
<tr>
<td>Witnessed (vs. non-witnessed)</td>
<td>0.42</td>
<td>&lt;.02</td>
<td>0.20–0.87</td>
</tr>
<tr>
<td>VT/VF (vs. PEA/asystole)</td>
<td>0.59</td>
<td>.3</td>
<td>0.22–1.55</td>
</tr>
<tr>
<td>Witnessed (vs. non-witnessed)</td>
<td>0.59</td>
<td>.3</td>
<td>0.22–1.55</td>
</tr>
<tr>
<td>Age</td>
<td>1.04</td>
<td>.08</td>
<td>0.99–1.10</td>
</tr>
<tr>
<td>Male</td>
<td>1.14</td>
<td>.7</td>
<td>0.63–2.07</td>
</tr>
<tr>
<td>HT (vs. ST) Interval of CPR to ROSC</td>
<td>0.99</td>
<td>1.0</td>
<td>0.49–2.00</td>
</tr>
<tr>
<td>Interval of CA to ROSC</td>
<td>1.06</td>
<td>&lt;.01</td>
<td>1.03–1.10</td>
</tr>
<tr>
<td>Interval of CPR to ROSC</td>
<td>1.07</td>
<td>&lt;.01</td>
<td>1.04–1.11</td>
</tr>
</tbody>
</table>

IH, in-hospital; OOH, out-of-hospital; CI, confidence interval; CA, cardiac arrest; VT, ventricular tachycardia; VF, ventricular fibrillation; PEA, pulseless electrical activity; HT, hypothermia therapy; ST, standard therapy; CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation.

**Variable Odds Ratio**

- **First whole blood pH**: 0.01
- **Initial glucose 70–250 mg/dL**: 1
- **Initial glucose <70 mg/dL**: 3.36
- **Initial glucose >250 mg/dL**: 5.31
- **No epinephrine bolus during resuscitation**: 1
- **1–5 epinephrine doses**: 3.98
- **≥6 epinephrine doses**: 28.8
- **Number of inotropes first 24 hrs**: 1.48
- **OOH (vs. IH) location of CA**: 2.48
- **Cardiac (vs. asphyxia) etiology**: 0.16
- **Witnessed (vs. non-witnessed)**: 0.42
- **VT/VF (vs. PEA/asystole)**: 0.59
- **Age**: 1.04
- **Male**: 1.14
- **HT (vs. ST) Interval of CPR to ROSC**: 0.99
- **Interval of CA to ROSC**: 1.06
- **Interval of CPR to ROSC**: 1.07

**95% CI**

- **First whole blood pH**: 0.00–0.10
- **Initial glucose 70–250 mg/dL**: 1
- **Initial glucose <70 mg/dL**: 1.03–10.93
- **Initial glucose >250 mg/dL**: 2.67–10.53
- **No epinephrine bolus during resuscitation**: Reference group
- **1–5 epinephrine doses**: 1.96–8.09
- **≥6 epinephrine doses**: 3.43–241.6
- **Number of inotropes first 24 hrs**: 1.17–1.87
- **OOH (vs. IH) location of CA**: 1.35–4.53
- **Cardiac (vs. asphyxia) etiology**: 0.04–0.60
- **Witnessed (vs. non-witnessed)**: 0.20–0.87
- **VT/VF (vs. PEA/asystole)**: 0.22–1.55
- **Age**: 0.99–1.10
- **Male**: 0.63–2.07
- **HT (vs. ST) Interval of CPR to ROSC**: 0.49–2.00
- **Interval of CA to ROSC**: 1.03–1.10
- **Interval of CPR to ROSC**: 1.04–1.11
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