Clinical paper

Does induction of hypothermia improve outcomes after in-hospital cardiac arrest?∗

Graham Nichol a, b, *, Ella Huszti a, Francis Kim a, c, Deborah Fly a, Sam Parnia d, Michael Donnino e, Tori Sorenson a, Clifton W. Callaway f, g

For the American Heart Association Get With The Guideline-Resuscitation Investigators

a University of Washington-Harborview Center for Prehospital Emergency Care, United States
b Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA, United States
c Division of Cardiology, Department of Medicine, University of Washington, Seattle, WA, United States
d Department of Medicine Stony Brook Medical Center, Stony Brook, NY, United States
e Center for Resuscitation Science, Departments of Emergency Medicine and Critical Care, Beth Israel Deaconess Medical Center, Boston, MA, United States
f Department of Emergency Medicine, University of Pittsburgh, Pittsburgh, PA, United States
g Department of Pharmacology and Chemical Biology, University of Pittsburgh, Pittsburgh, PA, United States

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ABSTRACT

Introduction: Hypothermia improves neurologic recovery compared to normothermia after resuscitation from out-of-hospital ventricular fibrillation, but may or may not be beneficial for patients resuscitated from in-hospital cardiac arrest. Therefore, we evaluated the effect of induced hypothermia in a large cohort of patients with in-hospital cardiac arrest.

Methods: Retrospective analysis of multi-center prospective cohort of patients with in-hospital cardiac arrest enrolled in an ongoing quality improvement project. Included were adults with a pulseless event in an in-patient hospital ward of a participating institution who achieved restoration of spontaneous circulation between 2000 and 2009. The exposure of interest was induced hypothermia. The primary outcome was survival to discharge. The secondary outcome was neurological status at discharge. Analyses evaluated all eligible patients; those with a shockable rhythm; or those with endotracheal tube inserted after resuscitation; and the effect of no hypothermia versus hypothermia (lowest temperature > 32 °C but < 34 °C) versus overcooled (≥32 °C). Associations were assessed using propensity score methods.

Results: Included were 8316 patients with complete data, of whom 214 (2.6%) had hypothermia induced and 2521 (30%) survived to discharge. Of patients reported to receive hypothermia, only 40% were documented as achieving a temperature between 32 °C and 34 °C. Adjusted for known potential confounders using propensity score methods, induced hypothermia was associated with an odds ratio of survival of 0.90 (95% confidence interval: 0.65, 1.23; p-value = 0.49) compared to no hypothermia. Induced hypothermia was associated with an odds ratio of neurologically-favorable survival of 0.93 (95% confidence interval: 0.65, 1.32; p-value = 0.68) compared to no hypothermia. For patients with shockable first-recorded rhythm, induced hypothermia was associated with an odds ratio of survival of 1.43 (95% confidence interval: 0.68, 3.01; p-value = 0.35) compared to no hypothermia.

Conclusion: Hypothermia is induced infrequently in patients resuscitated from in-hospital cardiac arrest with only 40% achieving target temperatures. Induced hypothermia was not associated with improved or worsened survival or neurologically-favorable survival. The lack of benefit in this population may reflect lack of effect, inefficient application of the intervention, or residual confounding. High-quality controlled studies are required to better characterize the effect of induced hypothermia in this population.

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1. Introduction

Hypothermia may reduce production of deleterious molecules, cerebral oxygen demand, and intracranial pressure in patients resuscitated from cardiac arrest, and thereby the final extent of their neurologic injury.1 Two trials showed hypothermia improved neurologic function versus normothermia in patients resuscitated from out-of-hospital ventricular fibrillation.2,3

∗ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2012.12.009.

* Corresponding author at: Box 359727, 325 Ninth Avenue, Seattle, WA 98104, United States.
E-mail address: nichol@u.washington.edu (G. Nichol).
The burden of in-hospital and out-of-hospital cardiac arrest are similar. While the physiology of brain injury is similar regardless of the location of arrest, patients resuscitated from in-hospital cardiac arrest (IHCA) are more likely than those resuscitated from out-of-hospital arrest to die with multiple organ failure.9 Thus, current care guidelines recommend induction of hypothermia after resuscitation regardless of the location of arrest.9 But no large observational study or trial has evaluated induced hypothermia in patients resuscitated from IHCA. We evaluated the effect of hypothermia in this population.

2. Methods

This study was approved by the Get With the Guidelines-Resuscitation (GWTG-R) scientific advisory board. The University of Washington Institutional Review Board (IRB) determined that this retrospective analysis of deidentified data was exempt from IRB review.

3. Study design

We used data from GWTG-R, an ongoing quality improvement project for IHCA. Participating hospitals voluntarily report data regarding in-hospital resuscitations as identified by an emergency resuscitation response by medical personnel and a resuscitation record. In GWTG-R, cardiac arrest is defined as unresponsive, apnea, and absence of a central pulse. The AHA provides quality control and oversight for all GWTG-R data collection, analysis, and reporting. Additional details regarding the study design, data collection, and quality oversight of GWTG-R were described elsewhere.5,10,11

4. Patient population

Included were adults who had IHCA between 2000 and 2009 in the general in-patient hospital ward and achieved restoration of spontaneous circulation. For an admission containing multiple cardiac arrest events, only the first arrest was included. Both primary and secondary analyses excluded patients who arrested in emergency departments, intensive care units, operating rooms, procedure areas, or post-procedural areas at the time of their arrest due to clinical circumstances associated with these environments that differ from the general inpatient hospital environment. Also excluded were patients with traumatic arrest. Furthermore, only patients with complete data for all variables used in the propensity score models were included in the analyses. All analyses excluded patients with unknown time of arrest due to the inability to ascertain key time-sensitive components in resuscitation response.

5. Exposure and outcomes

The primary exposure of interest was induced hypothermia after resuscitation. In GWTG-R, this was elicited as “Was induced hypothermia initiated after return of circulation ... achieved?” without any specific definition of hypothermia. Sensitivity analyses cross-validated “induced hypothermia” by confirming that the lowest temperature in the first 24 h post event was ≤ 34°C among patients treated between 2004 and 2009, when temperature data were included in GWTG-R.

The primary outcome was survival to discharge, expressed as the proportion of included patients who survived to hospital discharge. We tested the main hypothesis that survival to discharge was identically distributed between no hypothermia versus induced hypothermia after resuscitation from cardiac arrest.

The secondary outcome was neurologically-favorable survival, defined as the proportion of patients with cerebral performance category (CPC) score ≤ 2 at hospital discharge.12 We tested the secondary hypothesis that neurologically-favorable survival was identically distributed between treatment groups after resuscitation.

Post hoc secondary analysis evaluated the subgroup of patients who had a first recorded rhythm that was shockable (i.e. ventricular fibrillation, pulseless ventricular tachycardia or shockable by automated external defibrillator), because the prognosis of patients with cardiac arrest is associated with rhythm; as well as those who underwent endotracheal intubation post arrest as a surrogate for coma, because no objective assessment of post-resuscitation consciousness is included in GWTG-R.

Finally, post hoc secondary analyses compared survival and neurologically-favorable survival between patients with no hypothermia versus induced hypothermia (lowest temperature > 32°C and ≤ 34°C within 24 h post event) versus overcooled (lowest temperature < 32°C), as overcooling is associated with poor prognosis.13

6. Data analysis

Baseline patient characteristics were summarized descriptively. The association between exposure and outcome was determined by covariate adjustment using propensity scores (PS).14,15 This method uses logistic regression to predict the probability that an individual patient was exposed to the intervention of interest (e.g., hypothermia), with adjustment for factors recognized as potential confounders based on prior studies. The latter included: age, gender, race (white, black, other), prior residence, ethnicity (Hispanic vs. not), witnessed status, response time intervals, initial cardiac rhythm, whether ROSC was achieved within 5 min, admitting diagnosis (presence or absence of heart failure or myocardial infarction at admission), interventions in place prior to arrest (monitored versus not monitored) and year of event. PS models were repeated for the secondary outcome of neurologically-favorable survival. Weighted conditional standardized differences (WCSD) assessed whether the PS model was correctly specified, i.e. whether exposed and unexposed subjects with similar PS had similar distributions of baseline covariates.16 WCSD less than 0.1 are interpreted as suggesting good balance in a model.

All p values were expressed as two-sided, with values of p < 0.05 considered statistically significant. All analyses were performed using S-Plus 6.0 software (Tibco Software Inc., Palo Alto, CA).

7. Results

10,860 patients were eligible for inclusion in the study (Fig. 1). 8216 (76.6%) patients from 454 hospitals had complete data and were used in the analysis. Patient demographics and clinical characteristics were summarized in Table 1. Patients had mean age of 67 years, and 52% had male gender. 73% were white, and less than 6% were Hispanic. The majority lived at home prior to the event, while only 8% resided in an acute care facility. 27% were monitored before the event, and 59% of events were witnessed. About one in five patients was admitted with heart failure or myocardial infarction. 13% had a first recorded rhythm that was shockable. The response of staff to the arrest was immediate for at least 75% of patients. Less than a quarter of patients (23%) achieved ROSC within 5 min of initiation of compressions. All WCSD values were smaller than 0.1, except for gender (Table 1).

214 (2.6%) patients were reported to have received hypothermia in 100 (22%) hospitals. 2521 (30%) survived to discharge. 58 (27.1%) of the hypothermia group survived to discharge compared to 2454
Overall 1631 (20%) survived to discharge with a CPC score ≤ 2. Forty (18.7%) of the hypothermia group survived with CPC ≤ 2 compared to 1591 (20.1%) of the no hypothermia group. The unadjusted OR for neurologically-favorable survival was 0.91 [95% CI: 0.65, 1.30; p-value = 0.60] with induced versus no hypothermia. The propensity-adjusted OR for neurologically-favorable survival was 0.93 [95% CI: 0.65, 1.32; p-value = 0.68] with induced versus no hypothermia (Table 2).

6638 patients (80%) underwent endotracheal tube insertion post event. Of these, 25.6% survived to discharge and 16.1% were discharged with a CPC score ≤ 2. Among those intubated, the propensity-adjusted OR for survival was 0.91 [95% CI: 0.65, 1.28; p-value = 0.61] with induced hypothermia versus no hypothermia; the adjusted OR for neurologically-favorable survival was 0.96 [95% CI: 0.63, 1.44; p-value = 0.83] (Table 3).

Of 1374 patients with a shockable rhythm, 48% survived to discharge and 33% had a CPC score ≤ 2. Among patients with a shockable rhythm, the propensity-adjusted OR for survival was 1.43 [95% CI: 0.68, 3.01; p-value = 0.35] with induced hypothermia versus no hypothermia; the propensity-adjusted OR for neurologically-favorable survival was 1.26 [95% CI: 0.56, 2.73; p-value = 0.56] (Table 4).

Among induced hypothermia patients, 86 (40.2%) had a documented temperature between 32°C and 34°C consistent with achieving therapeutic hypothermia. 24 (11.2%) patients were overcooled (i.e. recorded temperature lower than 32°C), while 54 (25.2%) were undercooled (i.e. recorded temperature higher than 34°C). 50 (23.4%) subjects were missing temperature information. Since almost one-half of hypothermia patients were either missing valid temperature values or had potentially misreported values, we do not report comparisons of outcomes for overcooled and therapeutically cooled, because we consider these estimates potentially biased and unstable.

8. Discussion

In this retrospective analysis of patients with ICHA, only 2.6% of patients had hypothermia induced after resuscitation. A majority of treated patients were not documented as achieving the intended range of hypothermia or were overcooled. Induced hypothermia was not associated with survival or neurologic outcome.

Prior trials that reported benefit with induced hypothermia in patients resuscitated from cardiac arrest were conducted in different populations. The HACA trial included 275 comatose adults resuscitated from witnessed out-of-hospital ventricular fibrillation or non-perfusing ventricular tachycardia. Patients were randomly

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N=8316)</th>
<th>Induced hypothermia (N=214)</th>
<th>No induced hypothermia (N=8102)</th>
<th>p-value</th>
<th>Weighted conditional standardized difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>67.2 (15.1)</td>
<td>61.6 (16.9)</td>
<td>67.4 (15.0)</td>
<td>&lt;0.001</td>
<td>0.03</td>
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<td>Male, sex, %</td>
<td>52.5</td>
<td>55.6</td>
<td>52.5</td>
<td>0.40</td>
<td>0.14</td>
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<td>Race, %</td>
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<td></td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>White</td>
<td>72.6</td>
<td>64.9</td>
<td>72.8</td>
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<tr>
<td>Black</td>
<td>23.6</td>
<td>29.4</td>
<td>23.5</td>
<td>0.03</td>
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<tr>
<td>Other</td>
<td>3.8</td>
<td>5.6</td>
<td>3.7</td>
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<tr>
<td>Ethnicity, Hispanic, %</td>
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<td>7.0</td>
<td>5.6</td>
<td>0.45</td>
<td>0.05</td>
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<tr>
<td>Prior residence, %</td>
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<td></td>
<td>0.60</td>
<td>0.03</td>
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<tr>
<td>Home</td>
<td>75.1</td>
<td>78.0</td>
<td>75.1</td>
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<tr>
<td>Hospital or other acute care</td>
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<td>7.5</td>
<td>8.1</td>
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<td></td>
</tr>
<tr>
<td>Other</td>
<td>16.8</td>
<td>14.5</td>
<td>16.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Event monitored, %</td>
<td>26.9</td>
<td>21.5</td>
<td>27.1</td>
<td>0.08</td>
<td>0.01</td>
</tr>
<tr>
<td>CHF or MI at admission, %</td>
<td>18.5</td>
<td>15.4</td>
<td>18.6</td>
<td>0.27</td>
<td>0.02</td>
</tr>
<tr>
<td>Initial rhythm: VF or PVT, %</td>
<td>12.2</td>
<td>14.0</td>
<td>12.2</td>
<td>0.48</td>
<td>0.02</td>
</tr>
<tr>
<td>Event witnessed, %</td>
<td>58.5</td>
<td>52.8</td>
<td>58.6</td>
<td>0.10</td>
<td>0.06</td>
</tr>
<tr>
<td>RTI (min), median (IQR)</td>
<td>0.0 (0.0–0.0)</td>
<td>0.0 (0.0–0.0)</td>
<td>0.0 (0.0–0.0)</td>
<td>0.47</td>
<td>0.04</td>
</tr>
<tr>
<td>Time to ROSC &gt; 5 min, %</td>
<td>76.9</td>
<td>83.6</td>
<td>74.7</td>
<td>0.007</td>
<td>0.04</td>
</tr>
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</table>
allocated to normothermia, and placed on a conventional hospital bed, or hypothermia, and cooled to a target temperature of 32°C to 34°C within 6 h using an external cooling tent. The hypothermia group had greater survival (risk ratio 1.32; 95% CI: 1.04, 1.66) and a more favorable neurologic outcome (risk ratio, 1.40; 95% CI: 1.08, 1.81) than the normothermia group.

Bernard and colleagues included 77 unconscious adults resuscitated from out-of-hospital ventricular fibrillation.2 Core temperature was lowered to 33°C within 2 h using external cold packs then maintained for 12 h. The hypothermia group did not survive to discharge more than the normothermia group (odds ratio for survival 1.04; 95% CI: 0.38, 2.87). They were discharged to home or to a rehabilitation facility more often than the normothermia group (odds ratio for good outcome, 5.25; 95%CI: 1.47, 18.76).

These trials were pooled with smaller trials.17,18 The pooled results suggested that induced hypothermia significantly improved neurologic outcome (RR 1.55; 95% CI: 1.22, 1.96) compared to no hypothermia.17 But the pooled estimates of the effect of hypothermia on survival differed according to which patients were or were not included in the analysis, suggesting that the effects of hypothermia may not be robust.

Multiple cohort studies report associations between induction of hypothermia and good outcomes after resuscitation from cardiac arrest.19–21 Whether this relationship is causal is unclear because of the non-random treatment assignment and small sample size of these studies. A European registry reported 79% of 650 comatose patients in 19 sites received induced hypothermia.22 45% of the hypothermia group had favorable neurologic outcome compared to 32% of the non-hypothermia group. However, the baseline characteristics of the hypothermia and non-hypothermia groups differed.

The Hypothermia Registry reported that 86% of 1108 patients comatose after resuscitation from cardiac arrest received induced hypothermia.23,24 48% of the hypothermia group had favorable neurological outcome at 6 months compared to 31% of the non-hypothermia group. Again, the baseline characteristics of the treatment groups differed.

In the Dutch National Intensive Care Evaluation database,25 5317 patients received intensive care after cardiac arrest. 29% were treated before and 71% after implementation of a protocol to induce hypothermia. The adjusted odds ratio for survival to discharge with versus without hypothermia was 0.80 (95% CI: 0.65, 0.98).

Collectively the present and prior studies provide a mixed picture of the effect of hypothermia in patients with IHCA. Randomized trials that monitored treatment adherence observed that hypothermia improved outcomes compared to no hypothermia after out-of-hospital arrest.2,3 In contrast, the lack of benefit or harm observed in the present retrospective analysis is associated with lack of documented achievement of a therapeutic temperature range. We attempted to evaluate treatment adherence through sensitivity analysis but 48% of those stated to receive hypothermia were not documented to achieve a temperature under 34°C or did not have any temperature reported. It seems plausible that adherence may have been poor or data entry incomplete. Without active monitoring of adherence to temperature targets, we believe that the absence of evidence of benefit of induced hypothermia in this study does not connotes evidence of the absence of its benefit in this population.26 Thus differences between the results of the present and prior results can be reconciled.

This study has some strengths. First, the parent quality improvement project uses standardized Utstein-style definitions of baseline characteristics, and process and outcome of care.27 Data accuracy is ensured by certification of hospital staff and use of standardized software with range and logic checks for data completeness and accuracy.28

Second, we used rigorous methods to adjust for non-random allocation of patients to treatment. The usual approach to analyzing a binary outcome (e.g. survival) is logistic regression. An indicator for the exposure of interest (e.g. hypothermia) is included as a predictor along with known covariates to adjust for baseline differences. This assumes that relevant baseline factors have been measured and that outcomes were correctly specified. It is claimed that PS methods address potential misclassification of the response by reducing bias, albeit at the expense of precision.29–31 A third approach uses instrumental variables to predict exposure, then evaluates the relationship between differences in outcome as a function of differences in exposure. A valid instrument is neither associated with unmeasured confounders nor associated with outcome apart from the relationship between exposure and outcome.32 A potential advantage of using instrumental variables is that they adjust for unmeasured confounders, whereas regression and propensity score methods do not. We sought to use instrumental variables based on the geographic region of the participating hospital for this analysis, but determined that this approach lacked credibility because of the strong regional variation in outcome after cardiac arrest.6 We believe that methods used in this analysis are the strongest methods available to adjust for

<table>
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<th>Table 2</th>
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<tr>
<td>Effects of hypothermia versus no hypothermia on survival to discharge and neurologically-favorable survival to discharge among all included patients (N = 8316).</td>
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<table>
<thead>
<tr>
<th>Effect</th>
<th>Unadjusted odds ratio (OR) [95% confidence interval]</th>
<th>Unadjusted p-value</th>
<th>Adjusted odds ratio (OR) [95% confidence interval]</th>
<th>Adjusted p-value</th>
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</thead>
<tbody>
<tr>
<td>Survival to discharge</td>
<td>0.83 [0.61, 1.12]</td>
<td>0.29</td>
<td>0.90 [0.65, 1.23]</td>
<td>0.49</td>
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<tr>
<td>Neurologically-favorable</td>
<td>0.91 [0.65, 1.30]</td>
<td>0.60</td>
<td>0.93 [0.65, 1.32]</td>
<td>0.68</td>
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<tr>
<td>survival to discharge</td>
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<th>Table 3</th>
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<tr>
<td>Effects of hypothermia versus no hypothermia on survival to discharge and neurologically-favorable survival to discharge among patient intubated after resuscitation (N = 6638).</td>
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<thead>
<tr>
<th>Effect</th>
<th>Unadjusted odds ratio (OR) [95% confidence interval]</th>
<th>Unadjusted p-value</th>
<th>Adjusted odds ratio (OR) [95% confidence interval]</th>
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<tbody>
<tr>
<td>Survival to discharge</td>
<td>0.92 [0.65, 1.30]</td>
<td>0.98</td>
<td>0.91 [0.65, 1.28]</td>
<td>0.61</td>
</tr>
<tr>
<td>Neurologically-favorable</td>
<td>0.99 [0.66, 1.48]</td>
<td>0.97</td>
<td>0.96 [0.63, 1.44]</td>
<td>0.83</td>
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<td>survival to discharge</td>
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<th>Table 4</th>
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<tr>
<td>Effects of hypothermia versus no hypothermia on survival to discharge and neurologically-favorable survival to discharge among patients with shockable rhythm (N = 1374).</td>
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<thead>
<tr>
<th>Effect</th>
<th>Unadjusted odds ratio (OR) [95% confidence interval]</th>
<th>Unadjusted p-value</th>
<th>Adjusted odds ratio (OR) [95% confidence interval]</th>
<th>Adjusted p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to discharge</td>
<td>1.67 [0.79, 3.50]</td>
<td>0.39</td>
<td>1.43 [0.68, 3.01]</td>
<td>0.35</td>
</tr>
<tr>
<td>Neurologically-favorable</td>
<td>1.40 [0.66, 2.87]</td>
<td>0.37</td>
<td>1.26 [0.56, 2.73]</td>
<td>0.56</td>
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<td>survival to discharge</td>
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non-random differences in the baseline characteristics of treatment groups.

Third, the overall sample size of this study was larger than prior published studies of the effect of hypothermia after IHCA. As such, it provides some precision in the estimate of the effect of hypothermia in the real world. This study has some limitations. First, use or non-use of hypothermia was based on self-report rather than prospective monitoring. Importantly, a high proportion of patients were not documented to have achieved a temperature within the therapeutic range of hypothermia. Adults with spontaneous temperature lability or fever after resuscitation from cardiac arrest have worse outcomes compared with those who maintain normothermia. Hypothermia is a multifaceted rather than discrete intervention. At the time of resuscitation from out-of-hospital arrest, many patients are already mildly hypothermic with core temperatures between 35°C and 35.5°C. After restoration of circulation, patients warm within a few hours unless specific hypothermia interventions are instituted. Multiple methods of inducing hypothermia are used, although differences in the effect of surface and endovascular methods appear to be not large. Neurovascular paralysis and sedation can reduce shivering or other compensatory reflexes. The key trials of induced hypothermia after cardiac arrest utilized 12h² or 24h² of hypothermia. Unintentional overcooling below the target temperature range of 32–34°C is common, and associated with increased risk of adverse events. Thus, it is plausible that the lack of benefit of hypothermia observed in this study reflects incomplete or inconsistent application of the intervention rather than lack of effect. Second, we lacked information about whether patients were conscious after resuscitation. A multicenter study of patients resuscitated from cardiac arrest suggested better neurologic status before induction of hypothermia was associated with better survival. As well, a single-center study of patients with cardiac arrest treated at a resuscitation center of excellence suggested better organ function or neurologic status at hospital or intensive care arrival was associated with better survival. Induced hypothermia is usually only administered to patients who are unconscious as those who are conscious have had a brief course of cardiac arrest, and a favorable prognosis. Application of induced hypothermia to patients in this study could reflect confounding by indication. Patients who were unconscious were selected by their physicians to receive hypothermia and had a poorer prognosis than those who were conscious (and not selected to receive hypothermia). Our use of PS methods adjusted for known effect modifiers, but this may be insufficient due to incomplete correction for known factors and lack of correction for relevant but unmeasured factors. Uncontrolled residual bias has been proposed as the reason for discordance between observational and randomized estimates of cardiovascular therapies.

Third, other components of post-resuscitation care are associated with survival or good neurologic outcome. Time from restoration of circulation after out-of-hospital cardiac arrest to initiation of hypothermia in a high-volume hospital with a special interest in cardiac care was significantly associated with survival. Among patients resuscitated from out-of-hospital cardiac arrest in a single city, those who underwent coronary angiography within 6h of arrest had better survival than those who did not. Among patients resuscitated from cardiac arrest and admitted to hospitals where physicians had agreed to not assess prognosis early in Arizona, more than 50% of patients had care withdrawn within 72h. The data analyzed in the present study lack detailed information about the timing of these post-resuscitation events. It is plausible that the effect of induced hypothermia in this study was modified by how these components of care were applied. As well, hypoxemia in the post-resuscitation phase was not assessed, and could have impacted on survival in this study.

Fourth, the hospitals that participate voluntarily in GWTG-R represent a minority of hospitals in the United States. The processes and quality of care as well as survival of patients with IHCA in participating hospitals may differ from those in non-participating hospitals.

9. Conclusion

Hypothermia is induced infrequently in patients resuscitated from IHCA. A minority of treated patients were reported as receiving hypothermia or achieving target temperatures. The observed absence of evidence of survival or neurological benefit in treated patients may be evidence of the absence of effect, or inefficient application of the intervention or residual confounding. Application of hypothermia should include monitoring of adherence to treatment targets. High-quality controlled studies are required to better characterize the effect of induced hypothermia after IHCA.

Conflict of interest statement

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome beyond those stated below.

Nichol has applied for a grant from the National Heart Lung Blood Institute to conduct a randomized trial of different durations of induced hypothermia in patients resuscitated from out-of-hospital cardiac arrest, with third-party cost sharing to be provided by C.R. Bard Inc., Covington, GA; Cincinatti Sub Zero, Cincinatti, OH; EMCOOLS Medical Cooling Systems AG, Vienna, Austria; Stryker Medical, Kalamazoo, MI; and ZOLL Circulation, Sunnyvale, CA.

Nichol has waived compensation to serve as co-principal investigator for an industry-sponsored trial of ultrafast hypothermia in patients with acute ST-elevation myocardial infarction (Velomedix Inc., Menlo Park, CA).

References


