Therapeutic hypothermia after cardiac arrest: Unintentional overcooling is common using ice packs and conventional cooling blankets

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Objectives: **Although therapeutic hypothermia for cardiac arrest survivors has been shown to improve neurologically intact survival, optimal methods to ensure controlled induction and maintenance of cooling are not clearly established. Precise temperature control is important to evaluate because unintentional overcooling below the consensus target range of 32–34°C may place the patient at risk for serious complications. We sought to measure the prevalence of overcooling (<32°C) in postarrest survivors receiving primarily noninvasive cooling.**

Design: **Retrospective chart review of postarrest patients.**

Setting: **Three large teaching hospitals.**

Patients: **Cardiac arrest survivors receiving therapeutic hypothermia.**

Interventions: **Charts were reviewed if primarily surface cooling was used with a target temperature goal between 32°C and 34°C.**

Measurements and Main Results: **Of the 32 cases reviewed, overcooling lasting for >1 hr was identified as follows: 20 of 32 patients (63%) reached temperatures of <32°C, 9 of 32 (28%) reached temperatures of <31°C, and 4 of 32 (13%) reached temperatures of <30°C. Of those with overcooling of <32°C, 6 of 20 (30%) survived to hospital discharge, whereas of those without overcooling, 7 of 12 (58%) survived to hospital discharge (p = not significant).**

Conclusions: **The majority of the cases reviewed demonstrated unintentional overcooling below target temperature. Improved mechanisms for temperature control are required to prevent potentially deleterious complications of more profound hypothermia. (Crit Care Med 2006; 34[Suppl.]:S490–S494)**

KEY WORDS: cardiac arrest; sudden cardiac death; hypothermia; resuscitation; body temperature regulation

The use of therapeutic hypothermia (32–34°C for 12–24 hrs) for comatose survivors of cardiac arrest has been endorsed by the American Heart Association and the International Liaison Committee on Resuscitation (1). Recent work has demonstrated that postarrest cooling may improve survival and neurologic outcomes (2–5). Although these investigations utilized formal protocols for cooling, little has been published regarding practical noninvestigational experience with such protocols (6), particularly the prevalence of unintentional overcooling (<32°C) that can occur with surface induction of hypothermia. This is clinically important because overcooling may be associated with atrial or ventricular arrhythmias and also with coagulopathy and increased risk of infection (7–11). Although two animal studies suggest that hypothermia to temperatures as low as 30°C may improve defibrillation success (12, 13), at temperatures of <30°C, electrical shocks and subsequent anti-arrhythmic therapies may be ineffective (14). Finally, the therapeutic benefit of hypothermia itself could conceivably be lessened by cooling outside of the target temperature range.

Establishing precise temperature control is likely to be dependent on the cooling method selected. A variety of techniques such as surface cooling (2, 3, 15, 16), endovascular catheters (17, 18), cooling caps/helmets (4, 19), cool intravascular fluid (18, 20), and cardiopulmonary bypass (21) have been used to therapeutically lower core body temperature in either clinical or experimental settings. Among these, surface cooling with

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a cooling blanket or ice bags is generally considered the least expensive and most widely used. However, one of the disadvantages of surface cooling is that it can be cumbersome to apply and titrate. Furthermore, unintentional overcooling can occur as peripheral and core thermal compartments cool at variable rates and equilibrate over time, and tissue metabolism slows relative to the amount of cooling applied (22, 23). We sought to measure the prevalence of overcooling (<32°C) and temperature variability in cardiac arrest survivors receiving therapeutic surface cooling.

METHODS

We conducted a retrospective chart review of cardiac arrest cases occurring at two hospitals in the United States (Chicago and Richmond) and one hospital in Europe (Bristol, UK). Institutional Review Boards at the University of Chicago Hospital and Virginia Commonwealth University Health System granted approval for this research project. In the UK, the Southmead Hospital study proposal was reviewed and granted exemption by the institutional chair of the ethics committee given maintenance of patient anonymity.

Charts were reviewed for either 1 yr (University of Chicago Hospital and Virginia Commonwealth University Health System) or 6 months (Southmead Hospital) between January 2003 to May 2005. Cases were identified by querying adult billing records for documentation of cardiopulmonary resuscitation or cardiac arrest (University of Chicago Hospital) or by querying an established hospital cardiac arrest database (Virginia Commonwealth University Health System and Southmead Hospital). Charts were included for review if the patients were ≥18 yrs of age, not pregnant, comatose postarrest, cooled primarily with a surface cooling technique for ≥18 hrs, and had a documented goal target temperature of 32–34°C. Patients were excluded if temperature was not documented at least every 1–2 hrs during cooling and rewarming or if cooling was terminated prematurely (before 18 hrs). A postresuscitation cooling protocol was used at Virginia Commonwealth University Health System. An institution-specific protocol was not utilized at Southmead Hospital or University of Chicago Hospital (although a cooling protocol now exists at University of Chicago Hospital).

At all three institutions, all decisions regarding care of the patient and implementation of therapeutic hypothermia (such as cooling and rewarming techniques, monitoring devices, and pharmacologic adjuncts) were made at the discretion of the medical team responsible for managing the patient. Standard advanced cardiovascular life support protocols were followed for all resuscitation efforts. All patients received postresuscitation cooling in the emergency department or intensive care unit, and none had cooling initiated in the prehospital setting. All patients were treated primarily with surface cooling using a mattress/blanket or ice bags, although some received supplemental cooling with 4°C fluid boluses intravenously or via hemofiltration. Ice bags were placed around the head and neck, in the axilla, or in the groin. A target temperature goal of 33°C was documented in all charts. A tympanic or bladder thermometer was used to record temperature every 1 to 2 hrs during active cooling. Rewarming in most patients occurred either passively or with a warm air mattress/blanket. While cooling and rewarming, patients were monitored for arrhythmias, infection, and coagulopathies.

Data analyses were performed using a spreadsheet application (Excel, Microsoft, Redmond, WA). Descriptive statistics (mean, SD) and chi-square analyses are primarily presented.

RESULTS

Therapeutic hypothermia was utilized in 32 patients after resuscitation from cardiac arrest. Patients were cooled after both in-hospital cardiac arrest (14 of 32 patients) and out-of-hospital cardiac arrest (18 of 32 patients). Average age was 61 yrs (range, 18–86 yrs), and 20 of 32 patients (63%) were men. Initial rhythms included ventricular fibrillation in 16 of 32 patients (50%), pulseless electrical activity in 13 of 32 (41%), and asystole in 3 of 32 (9%). The mean time from collapse to return of spontaneous circulation was 17.7 ± 15.0 mins (excluding five cases with no collapse time documented). The time course from return of spontaneous circulation to initiation of cooling was 2.6 ± 2.5 hrs, and then the time to reach 34°C was 3.4 ± 3.1 hrs (Table 1).

All patients were intubated before cooling and received hypothermia therapy with a cooling mattress or blanket. In

Table 1. Demographic characteristics of cooled patients (n = 32)

Age in years, mean (range)	61 (18–86)
Male sex, n (%)	20 (63)
Arrest location, n (%)	
In-hospital	14 (44)
Pre-hospital	18 (56)
Witnessed, n (%)	13 (41)
Initial cardiac rhythm, n (%)	
Ventricular fibrillation	16 (50)
Pulseless electrical activity	13 (41)
Asystole	3 (9)
Time in minutes to ROSC, mean ± SD	17.7 ± 15.0[a]
Time in hours from ROSC to cooling initiation, mean ± SD	2.6 ± 2.5
Time in hours from cooling initiation to 34°C, mean ± SD	3.4 ± 3.1

ROSC, return of spontaneous circulation.
[a]Data from 27 cases, as five did not have "down time" documented.

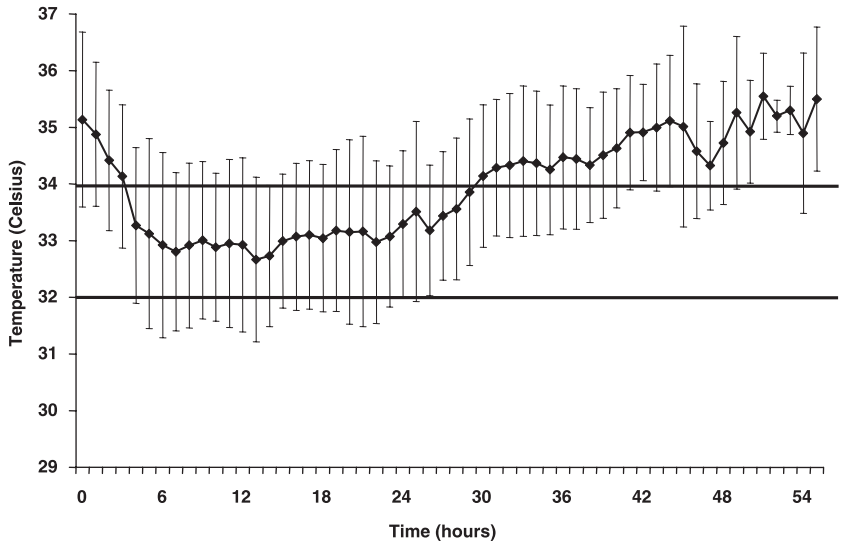

Figure 1. Mean temperature recordings for all patients. *Horizontal bars* mark the target temperature range of 32–34°C. Time 0 represents cooling initiation (n = 32).

addition, 5 of 32 of patients (16%) received a single 2-L bolus of 4°C saline intravenously during cooling initiation, and 2 of 32 (6%) received supplemental cooling via hemofiltration. Temperature was measured via either a tympanic thermometer in 18 of 32 patients (56%) or bladder thermometer in 14 of 32 (44%). The mean temperature before cooling initiation was 35.1°C ± 1.5°C. One patient was already within target range (33.1°C) when cooling was initiated. Average temperature recordings for all patients are shown in Figure 1.

Temperatures of <32°C persisted for ≥1 hr in 20 of 32 patients (63%). Of these patients, 9 of 32 (28%) reached temperatures of <31°C, and 4 of 32 (13%) reached temperatures of <30°C. Figure 2 illustrates examples of individual temperature recordings for two patients exhibiting unintentional overcooling. Figure 3 summarizes temperature variability in patients with overcooling. Of note, fluctuations in temperature of <32°C occurred throughout both the initiation and maintenance phase of cooling. Occurrences of overcooling were also distributed across institutions: University of Chicago Hospital, 8 of 12 patients (67%); Virginia Commonwealth University Health System, 9 of 14 (64%); and Southmead Hospital, three of six patients (50%).

Rebound hyperthermia (temperature of >38°C at 12–18 hrs after the end of active rewarming) developed in 7 of 32 patients (22%) and was treated with additional cooling. No patients exhibited significant arrhythmias requiring treatment during cooling or rewarming. Comfort care or do-not-resuscitate orders were established in 10 of 32 patients (31%) after achieving a temperature of 36°C who then died within the next 24 hrs. Of the patients with temperature overcooling, 6 of 20 (30%) survived to hospital discharge, whereas 7 of 12 (58%) of those without overcooling survived to hospital discharge (p = not significant). Overall, there was no statistically significant relationship between unintentional overcooling and initial temperature, presenting rhythm, arrest location, or utilization of a supplemental cooling method (data not shown), although the study was not designed to assess these interactions.

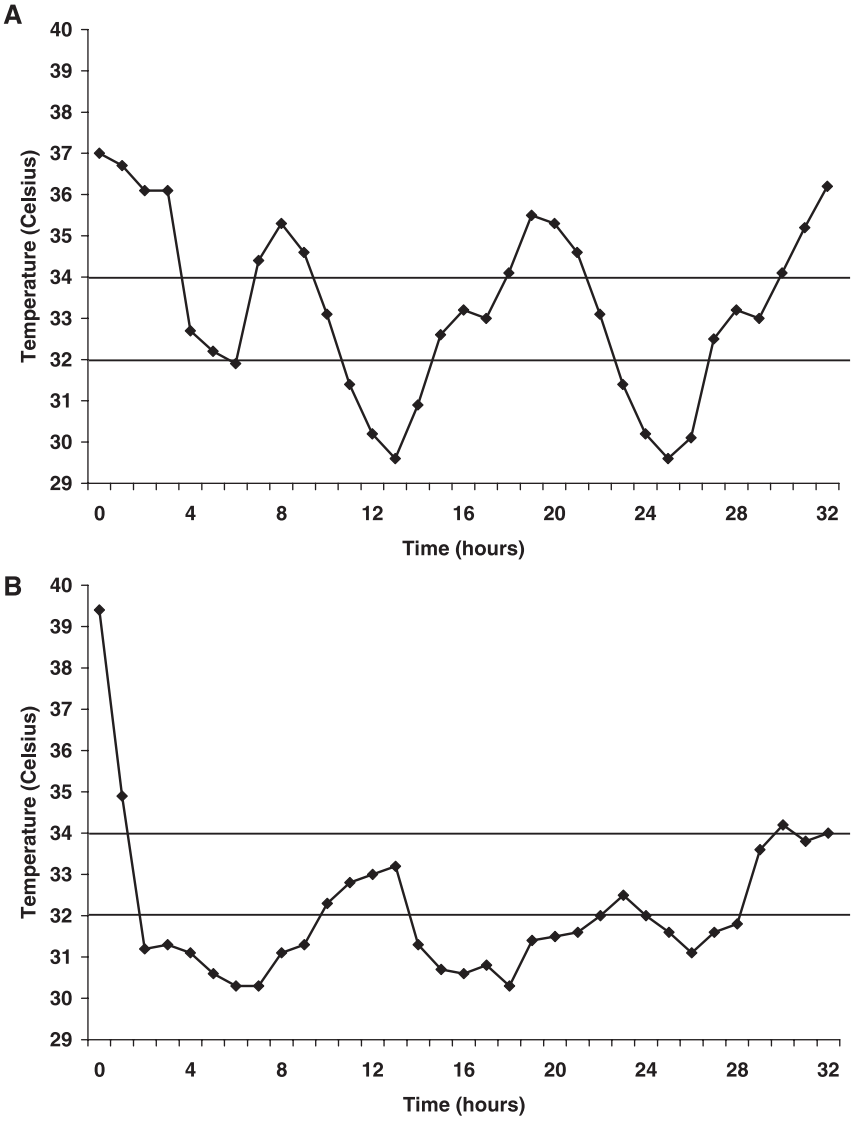

Figure 2. Individual patient temperature courses with overcooling. *Horizontal bars* mark the target temperature range (32–34°C). Note repeated fluctuations both above and below the target temperature range in both examples. *A*, patient with wide swings in temperature control; *B*, patient with persistent overcooling.

DISCUSSION

Our study emphasizes that maintaining precise temperature control with surface cooling in cardiac arrest survivors may be difficult and that unintentional overcooling is common. Our averaged temperature data suggest that patient temperatures were maintained within target range (Fig. 1). However, when viewed as individual cases (Fig. 2), a number of variations in temperature and overcooling become apparent. Furthermore, temperature fluctuations occurred often and throughout both the initiation and maintenance phases of cooling (Fig. 3). Overall, avoiding overcooling below the target range may be important clinically because adverse events likely increase when patients are cooled to <32°C (7–9, 24). In addition, the therapeutic benefit of hypothermia could conceivably be attenuated by overcooling outside the consensus target temperatures.

The factors leading to overcooling are likely multifactorial. Several reports have shown that critically ill patients and those with severe neurologic disorders exhibit difficulties with temperature regulation (25–27). Furthermore, patients receiving surface cooling may also be at an increased risk of overcooling because of problems with equilibration of the peripheral temperature with the core body temperature (22). A lack of appropriate guidelines for how to best titrate ice bags and cooling blankets to maintain a specific temperature range may also have contributed to the increased frequency of overcooling. Of note, it is unlikely that

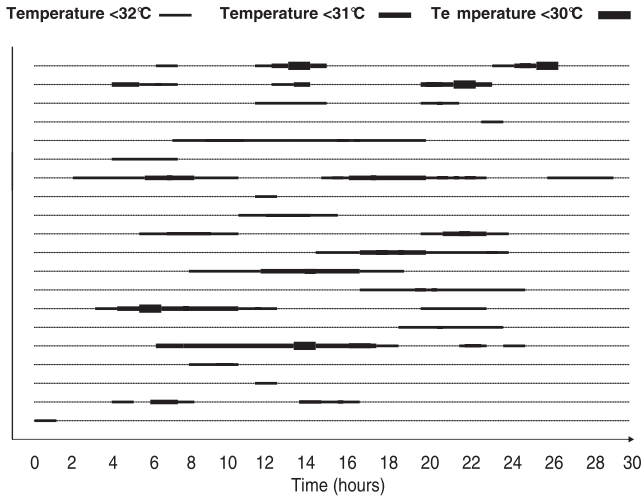

Figure 3. Each *horizontal line* along the *x-axis* represents the temperature course during the first 30 hrs for individual patients with overcooling. The *shaded horizontal bars* represent cooling below target temperature. The length of the bar correlates with the time the patient was at <32°C, and the width of the bar correlates with depth below 32°C. Notice that overcooling was not simply a phenomenon during cooling initiation but was seen throughout the cooling period. Furthermore, many patients had recurring hypothermia during the 30 hrs of cooling.

overcooling represented a learning-curve effect because cooling therapy for treatment of other conditions (such as hyperthermia) has been utilized at all three institutions. In addition, overcooled patients were distributed evenly throughout the study period.

Several other studies of postresuscitative cooling support our findings that temperature control is challenging. The Hypothermia After Cardiac Arrest group (3) initiated therapeutic hypothermia in 137 patients using a cooling mattress and bladder temperature probe. They reported that 93 of 132 patients (70%) required the addition of ice packs and that 19 of 132 (14%) never reached target temperature. Furthermore, cooling was terminated prematurely in two patients because of "problems with the cooling technique" and in three patients because of arrhythmias and hemodynamic instability. It is possible that once aggressively cooled to target temperature, some patients may have experienced temperatures of <32°C, but only aggregate data were presented. Patients with more precise temperature control may have experienced better outcomes and fewer complications than those with overcooling.

The difficulties of tight temperature control may not be limited to surface cooling. Al-Senani et al. (17) studied hypothermia in cardiac arrest survivors using a closed-loop endovascular catheter. Patients were cooled rapidly and maintained at an average of 32.7 ± 0.5°C. Overcooling occurred in several patients, with reported temperature recordings as low as 30.5°C.

In addition, in a current survey of physician utilization of cooling after cardiac arrest, many clinicians noted difficulties with temperature control, including both overcooling and rebound hyperthermia (28). Of note, the rebound hyperthermia may have been a physiologic response to the cooling or may represent postresuscitation pathophysiology because cardiac arrest patients are at risk for developing systemic inflammatory response syndrome (29).

Accurate induction and maintenance of therapeutic hypothermia is likely to be dependent on the cooling method selected and the adjustments made in response to ongoing temperature fluctuations. We have reported on temperature maintenance using surface cooling with a tympanic or bladder thermometer. This technique is appealing to many physicians using therapeutic hypothermia because materials such as ice bags and cooling blankets are easily accessible and inexpensive. Titration and continuous temperature measurement with these methods can be difficult, however. As temperature decreases, the optimal temperature point between 32°C and 34°C at which one should slow the cooling process is not well understood. Furthermore, a number of other factors, including patient age, weight, sex, and concomitant disease, affect temperature control. Feedback algorithms linking cooling devices with temperature monitors will likely allow for improved temperature control and less prevalence of overcooling. Greater awareness of differences in compartment (core vs. peripheral) cooling rates will also likely help improve temperature titration.

There are several limitations to this study inherent to retrospective chart review. The authors of this article were not involved in selecting patients or making clinical treatment decisions; however, the charts reviewed noted cooling goals of "33°C for 18 hrs," which are consistent with guidelines recommendations (1). Retrospective review and small sample size also prevent us from making conclusions about how brief periods of overcooling affected outcomes. It is possible that brief periods of overcooling may be harmful and lead to worse outcomes. Alternatively, overcooling may serve as a marker of underlying postarrest neurologic and temperature control instability and be associated with worse outcomes as an epiphenomenon. Of note, several patients had care withdrawn or were assigned do-not-resuscitate orders and died within 24 hrs after cooling and rewarming. This brief period for patient assessment after cooling may not have been adequate to determine potential neurologic recovery (30). Furthermore, high rates of unwitnessed arrest, prolonged time to return of spontaneous circulation, and high rates of pulseless electrical activity and asystole all likely contributed to low survival in our study population. It is likely that imprecise temperature control should be included among important factors contributing to poor outcomes after therapeutic hypothermia in cardiac arrest survivors.

CONCLUSIONS

External cooling methods may lead to overcooling and lower the threshold for adverse outcomes. As postarrest cooling will likely be used increasingly in coming years, it is important that further research is directed toward determining optimal cooling techniques and variables (31–33). Well-designed cooling protocols will also likely help cooling occur more safely and uniformly.

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