

A CHILLING REVIEW OF HYPOTHERMIA

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Translating Research into Practice

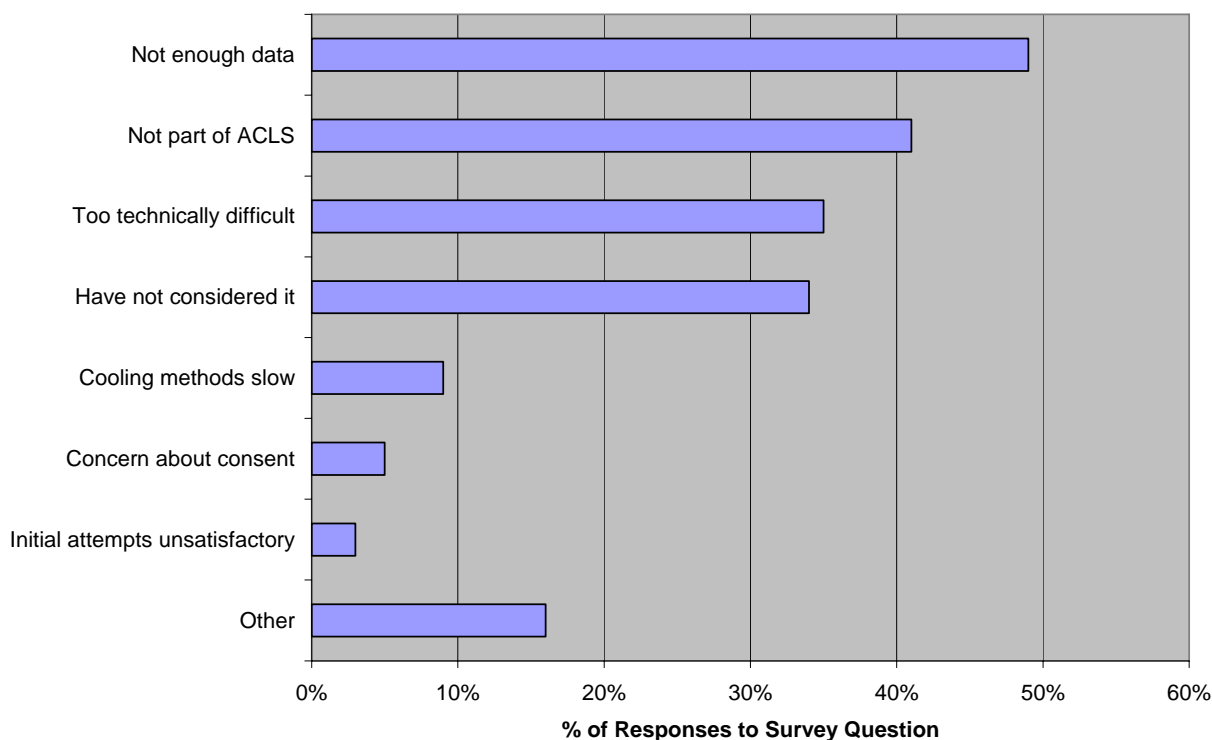
How good are healthcare providers at translating research into practice? In order to answer this question, I will use the example of therapeutic hypothermia (TH) for this newsletter issue. In October 2002 the International Liaison Committee on Resuscitation made the following recommendations on *Therapeutic Hypothermia After Cardiac Arrest*:¹

- Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was ventricular fibrillation (VF).
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.

These recommendations were based on the results of two prospective randomized trials comparing mild hypothermia with normothermia in comatose survivors of out-of-hospital cardiac arrest.^{2,3} It was shown that by treating 7 patients with TH, one life can be saved. Also, it takes treating 5 patients with TH to improve neurologic outcome. Both are highly significant findings.

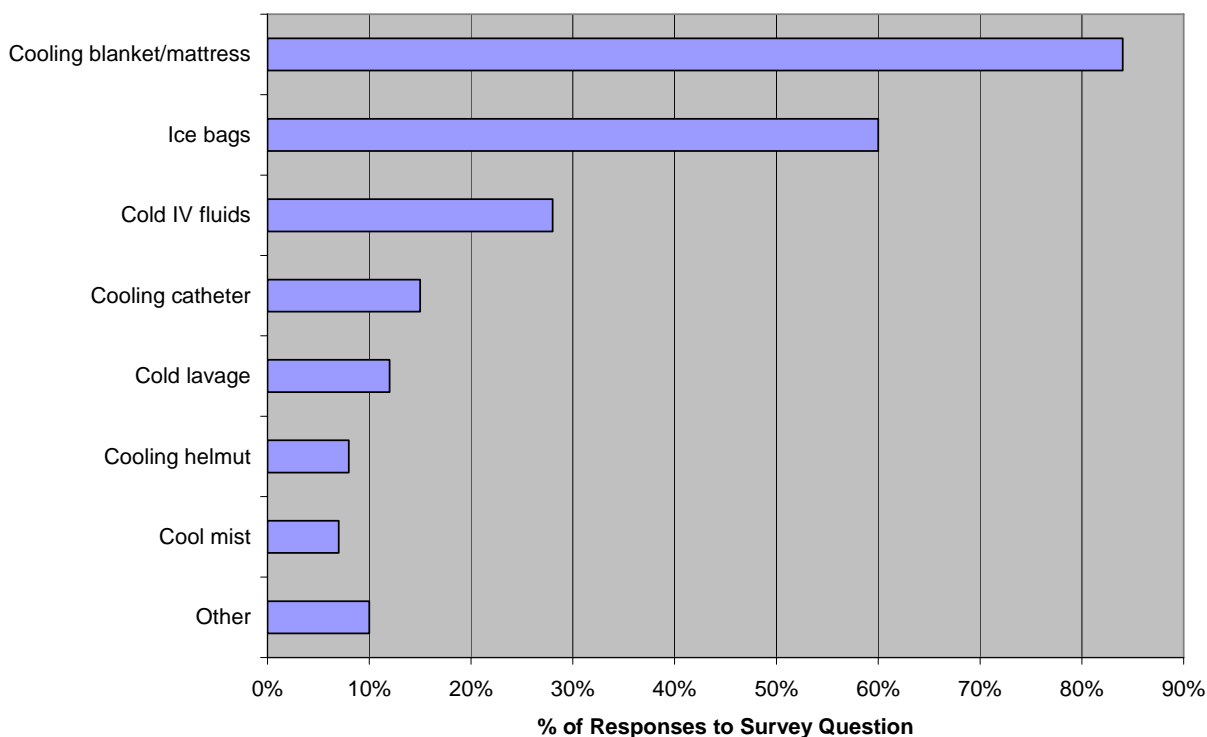
The University of Chicago conducted an Internet-based survey regarding TH utilization with physicians in the U.S. and elsewhere, employing a custom-designed survey tool with multiple-choice and free-response questions.⁴ Of the 2248 responses, 91% of the physicians practiced in the U.S., and most were attending physicians at teaching hospitals with >250 beds. Of all U.S. respondents 74% had never used TH, whereas 64% of non-U.S. respondents reported non-use. Reasons most often cited for non use are shown in Figure 1. Note that respondents were allowed to choose multiple answers; thus the total percentages add up to >100%.

Figure 1 Survey Responses to Why Therapeutic Hypothermia Not Used



Methods used to induce TH in the U.S. from results of this survey are reported in Figure 2. This survey shows that physicians caring for resuscitated patients report low rates of TH, and there are a number of impediments that were identified related to committing the research into actual practice in the U.S. The lack of post resuscitation care according to recognized international guidelines is disappointing – or one could say “chilling”.

Figure 2 Survey Responses to Induction Method for Therapeutic Hypothermia



The Evidence that Supports a Practice Change

There are three randomized controlled trials of TH with adult patients following cardiac arrest. The first was a feasibility study reported by Hachimi-Idrissi.⁵ Thirty patients with asystole or pulseless electrical activity (PEA) arrest were randomized to receive normothermia or cooling with a helmet to a bladder temperature of 34°C. Only 50% of these arrests were witnessed. The helmet was removed once mild hypothermia was achieved. No significant improvement was found in survival for the group with TH, though neurologic outcome improved.

The Hypothermia after Cardiac Arrest (HACA) Study Group reports on a multicenter trial in 9 centers in 5 European countries with patients who had been resuscitated following a witnessed VF/ventricular tachycardia (VT) arrest and randomly assigned to undergo TH with a target temperature of 32-34°C, measured in the bladder.³ TH was induced using a mattress to deliver cold air over the entire body, and ice packs were often added to maintain the lower temperature. The target temperature could not be achieved in 19 patients within the hypothermic group. The median interval between restoration of spontaneous circulation (ROSC) and the attainment of a temperature between 32-34°C was 8 hours. Seventy-five of the 136 patients in the hypothermia group had a favorable neurologic outcome (55%) (i.e. able to live independently and work at least part-time) measured at 6 months, as compared with 54 of 137 (39%) in the normothermia

group ($p=0.009$). Mortality at 6 months was 41% in the TH group compared to 55% in the normothermia group ($p=0.02$). The complication rate did not differ significantly between the two groups.

A third study was undertaken in 4 hospitals in Melbourne, Australia.² Seventy-seven patients with VF arrest were randomly assigned to either normothermia or TH with a core body temperature goal (pulmonary artery thermometry) of 33°C initiated in the field and reached within 2 hours using cold packs for 12 hours. Twenty-one of the 43 patients treated with TH (49%) survived and had a good outcome (i.e. they were discharged home or to a rehabilitation facility) as compared with 9 of the 34 treated with normothermia (26%), with a $p=0.046$. There was no difference in the frequency of adverse events.

In summary, only one of these studies (HACA) showed a statistically significant improvement in in-hospital mortality, but when the results were pooled by Cheung there was an overall decrease.⁶ All three studies showed improved neurologic outcome with TH.

Pathophysiologic Benefit of Therapeutic Hypothermia

Discharge rates following *in-hospital* resuscitation are poor, reported by the National Registry of CPR (NRCPR) to be 18% for adults.⁷ Even more dismal are the survival rates after *out-of-hospital* cardiac arrest, hovering around 4-9%.⁸ Less than 50% of those discharged are neurologically intact.⁹ Brain death or limitation of therapy through Do Not Resuscitate orders is often the cause of patient demise in the hospital.

Cerebral injury occurs after any condition in which there is inadequate blood flow to the brain for >5 minutes. The mechanisms involved are:

- Release of excitatory neurotransmitters
- Dysregulation of calcium homeostasis
- Free radical oxidation of cellular components

These biochemical cascades lead to mitochondrial damage and apoptosis, or programmed cell death. Neurologic damage continues to occur for a period of three days or longer after cardiopulmonary arrest; this has been labeled reperfusion injury.

Hypothermia is thought to play a neuroprotective role after ROSC by decreasing metabolic demand, decreasing the release of excitatory neurotransmitters, and decreasing the systemic inflammatory response. For each 1°C decrease in temperature, the cerebral metabolic rate decreases by 6-7%.¹⁰

Selection of Patients for Therapeutic Hypothermia

The inclusion/exclusion criteria from the original research studies mentioned above can be used to help in selection criteria when writing hospital protocols for TH. Their inclusion criteria included **all** of the following:

- Patients resuscitated from out-of-hospital witnessed arrest with VF/VT as the initial rhythm
- An estimated interval of 5-15 minutes from the patient's collapse to the first attempt at resuscitation by emergency medical service (EMS)
- An interval of no more than 60 minutes from collapse to ROSC
- Persistent coma after ROSC
- Endotracheal intubation with mechanical ventilation
- Adult age range

Excluded in the research studies were those with:

- Severe cardiogenic shock (systolic BP <90 mm Hg despite use of inotropes and fluids)
- Life-threatening arrhythmias
- Pregnancy
- A known coagulopathy
- Cause of coma other than cardiac arrest (e.g. head injury, drug overdose, cerebrovascular accident)
- Initial temperature < 30°C
- Pre-existing DNR code status

Expanding from these strict criteria, it seems reasonable for hospitals to consider for inclusion:

- Patients whose initial rhythm in arrest was asystole or PEA
- Patients whose arrest occurs in-hospital

The patient should have no existing multi-organ dysfunction, severe sepsis, or co-morbidities that will minimize the chance of meaningful survival. Thrombolytic therapy does not preclude the use of hypothermia. Some institutions exclude females under 50 years of age to avoid the potential of the patient being pregnant. But another approach is to conduct a quick pregnancy test in younger females since it would be a shame not to include this group. There are no studies with the pediatric population to date to guide use of TH following cardiac arrest in this age group. A recent abstract presented at the 2006 American Heart Association (AHA) Scientific Sessions by Ploj concluded that with the use of TH in diabetic patients mortality was significantly higher when compared to those who are not diabetic.¹¹ Further research is needed to determine if a different protocol would be helpful for this group of patients.

Timing of Introduction of Therapeutic Hypothermia

Delays in cooling diminish or even abrogate the beneficial effects of TH in experimental models.¹² But positive outcomes have been achieved when the target temperature was reached only after 4-6 hours. The University of Chicago survey learned that cooling took place primarily in the intensive care unit (ICU) for both the U.S. and non-U.S. respondents. Only a few respondents initiated cooling in the emergency department. It is stated that the cumbersome nature of the current methods used for cooling preclude use in the transport ambulance. Simpler methods can be applied in the ED such as keeping the temperature of the room low, removing clothes from the victim, and applying ice packs. If the patient is not quickly transferred to the ICU, the infusion of cold fluids can be started; see *Cooling Techniques* section.

There have been no **human** studies comparing outcomes when TH is applied earlier, but a swine study was reported at the 2006 AHA Scientific Sessions by Menegazzi at the University of Pittsburgh.¹³ They instrumented 30 swine, then assigned them to 3 groups (10 in each). VF was electrically induced and untreated for 8 minutes. Hypothermia was induced by rapid IV infusion of ice-cold normal saline (NS) at 30 ml/kg five minutes before VF in the PRE group and at the start of resuscitation in the DUR group. The NORM group got 30 ml/kg of body-temperature saline at the start of resuscitation. After 8 minutes of VF, two minutes of CPR was followed by delivery of drugs and 3 more minutes of CPR, with the first rescue shock given at 13 minutes of VF. ROSC occurred in 5/10 PRE, 7/10 DUR, and 4/10 NORM. Survival occurred in 5/10 PRE, 6/10 DUR and 3/10 NORM (DUR vs NORM p=0.30). It was concluded that intra-resuscitation

cooling doubled short-term survival compared to NORM. More research is needed in this area of timing the TH, along with investigation into practical methods for achieving hypothermia prior to arrival in the ICU.

Cooling Techniques

Techniques to induce and maintain hypothermia can be either non invasive or invasive. Those mentioned in literature are listed in Table 1.

Table 1 Cooling Techniques	
Non-Invasive Techniques	Invasive Techniques
<ul style="list-style-type: none"> ▪ Cooling blankets/pads ▪ Ice packs ▪ Caps or helmets ▪ Immersion in cold water ▪ Self-adhesive hydrogel cooling pads 	<ul style="list-style-type: none"> ▪ Infusion of cold IV fluids ▪ Heat exchange catheter ▪ Extracorporeal circulating cooled blood ▪ Retrograde jugular vein flush ▪ Nasal, nasogastric, lung & rectal lavage ▪ Peritoneal lavage with cold exchanges ▪ Intraventricular cerebral hypothermia

Surface cooling can be accomplished with circulating cold water blankets and cold air-forced blankets. These devices are usually already available in hospitals and care providers know how to operate them, but it takes 2 to 8 hours to reduce the core temperature to 32-34°C and titration of temperature can be difficult. A new generation device is the CritiCool™ in which the controller is set to the desired temperature and the CureWrap™ garment is applied.¹⁴ This one-piece garment adheres directly to the patient's body using medically approved adhesive and circulates tap water. The 3-dimensional surface coverage provides high heat exchange. See Figure 3.

Figure 3 CritiCool Therapy by MTRE



Figure 4 EMCOOLS Cooling Blanket



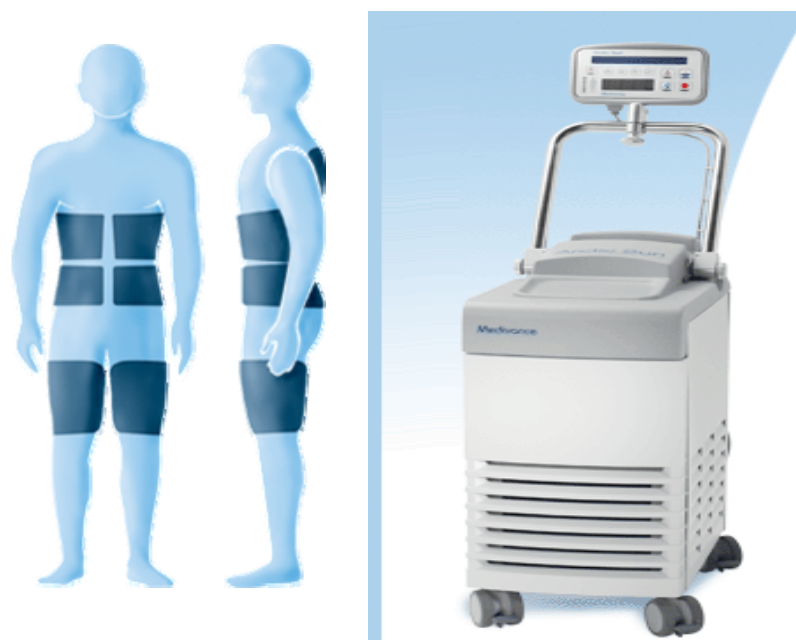
Another cooling blanket was discussed by Uray at the 2006 Resuscitation Science Symposium.¹⁵ The EMCOOLS® pad consists of multiple cooling elements that are filled with a combination of graphite/water and placed directly on the skin surface. See Figure 4. In a study with 8 cardiac arrest patients the cooling-blanket decreased temperatures from 35.8°C at baseline to 34.0°C within 37 (30-45) minutes, and to the target temperature of 33°C within 56

(51-62) minutes after initiation of cooling, resulting in a cooling rate of 3.3 (2.6-3.5)°C/hour. Under investigation is use of the device in the pre hospital setting since it is independent of an energy source.

Ice packs can easily be applied to the armpits, head/neck and groins, but the rate of core temperature decrease is only 0.9°C/hour. Caps and helmets have been used to cool the surface of the head and neck to create selective cerebral hypothermia in infants. Immersion in cold water is not practical. A new flexible surround suit system was described with domestic swine by Ohley at the 2006 AHA Scientific Sessions.¹⁶ It provides a thin 0.5 cm layer of circulating ice water in direct skin contact held between 0.5°C and 1.5°C. A pumping system was used to circulate the water volume of 20 liters at a rate of 15 liters/minute. The average time to decrease the temperature by 3°C was 13 minutes.

Medivance produces the non invasive Arctic Sun[®] Temperature Management System in which hydrogel-coated pads that circulate temperature-controlled water under negative pressure adhere to the patient's abdomen, back and thighs.¹⁷ The Energy Transfer Pads[™] provide direct thermal conduction through the skin. This is different than conventional water blankets or wraps, in which air is trapped between the cooling source and the skin, and the patient is cooled by cold air (convection). The Arctic Sun Control Module reacts to patient temperature (obtained using standard temperature probes) by automatically adjusting the circulating pad water temperature to achieve a preset patient target temperature. The cooling rate is reported to be 1.5°C/hour or better. See Figure 5.

Figure 5 Arctic Sun Temperature Management System by Medivance

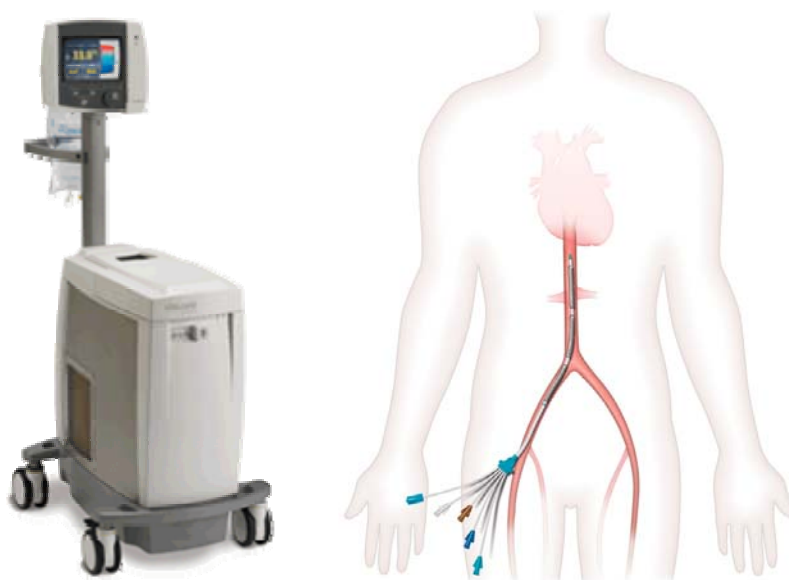


Bernard first described inducing hypothermia for 22 patients post out-of-hospital resuscitation with 30 ml/kg lactated Ringers solution that had been chilled to 4°C and infused over 30 minutes using a pressure bag via either a peripheral cannula or femoral venous catheter.¹⁸ This dropped the median core temperature from 35.5 to 33.8°C. There were significant improvements in mean

arterial blood pressure, renal function and acid-base analysis. He reported that there were no adverse effects of the rapid infusion of this volume of IV crystalloid fluid. A similar study followed by Virkkunen in which 30 ml/kg of iced Ringer's solution was infused at a rate of 100 ml/minute to 13 patients - except that it was administered in the pre hospital setting following resuscitation.¹⁹ The study with the largest number of patients using ice-cold IV fluid is by Polderman.²⁰ Hypothermia was induced in 134 patients with various types of neurologic injury by means of ice-water cooling blankets and infusion of 4°C saline (110 patients) or saline and colloids (24 patients). An average of 2340 ± 890 ml of fluids was infused in 50 minutes. Core temperatures decreased from $36.9 \pm 1.9^\circ\text{C}$ to $34.6^\circ\text{C} \pm 1.5^\circ\text{C}$ at 30 minutes and to $32.9 \pm 0.9^\circ\text{C}$ at 60 minutes. The conclusion from these studies is that induction of hypothermia by means of cold IV infusion is fast, efficacious, and safe. It should be followed by another method to maintain hypothermia, such as cooling blankets. Polderman used central venous catheters in all his patients, but rarely changed therapy based solely on these readings. So he concludes that cold-infusion therapy can be safely used without having central venous access, provided that the patient is intubated and mechanically ventilated. Contraindications to the infusion of cold IV fluid include patients in pulmonary edema and those with chronic renal failure and on dialysis who may be unable to excrete a large fluid load.²¹

An external heat exchange control device is available that circulates chilled saline to an indwelling venous line placed percutaneously in the patient - a closed-loop design. The special triple lumen intravascular catheter has 3 cooling membranes. Femoral, subclavian and internal jugular catheters may be used for this technique. Alzaga states that femoral catheters are preferred as dysrhythmias are more likely to occur when using subclavian or jugular routes.¹⁰ The device remotely senses patient temperature through standard probes and compares it to a user-selected target temperature, adjusting the temperature of the circulating sterile saline appropriately. In a feasibility study with the CoolGard 3000® device and Icy™ catheter, cooling averaged $0.8^\circ\text{C}/\text{hour}$, and it took 3 hours and 39 minutes to reach 33°C .²² Temperature can be tightly maintained, and rewarming can be controlled actively. Patient access for care is facilitated with this catheter-based technology, but there is a risk of infection and of bleeding at the insertion site. It is claimed that there are no external skin injuries that appear after external cooling, and less or no shivering compared to external cooling. Patient and system data are continuously stored, allowing recall and graphical display. A major limitation is the high cost of the device (list price \$32,500). See Figure 6. A similar device is the Celcius Control System™ and Accutrol™ catheter by INNERCOOL Therapies.

Figure 6 CoolGard 3000 with Icy femoral catheter by Alsius Corporation



Another invasive type of cooling is the use of devices which require circulation of blood through an extracorporeal circuit, allowing for rapid infusion of cold fluids, oxygenation of blood during resuscitation and rapid delivery of intravenous drugs. Soga from Japan reports on the use of an extracorporeal cooling method (KTEK-3, Kawasumi Company) to cool post resuscitation patients (who met the HACA inclusion criteria) to a target temperature of 34°C within 2 hours after the ROSC.²³ An IV infusion of 1500-2000 ml of extracellular fluid at 4°C was also delivered over 30 minutes immediately after emergency room arrival. The target temperature was maintained precisely for 24 hours when collapse-to-ROSC interval was within 20 minutes, 48 hours when that interval was 20-30 minutes, and 72 hours when that interval was more than 30 minutes. A total of 566 patients were enrolled; 30 were treated with the hypothermia and 539 were treated with normothermia. Among patients with VF/VT as an initial cardiac rhythm, 17 of the 22 (77.3%) patients in the hypothermia group had a favorable neurological outcome, as compared with 80 of 207 (38.6%) patients in the normothermia group ($p<0.001$). In addition among patients with PEA or asystole, the hypothermia group was associated with an improved favorable neurological outcome compared with the normothermia group (25% vs 7%, $p=0.05$). This technology can only be employed in centers where the extracorporeal device and trained staff are available 24 hours a day.

Retrograde jugular vein flush and intraventricular cerebral hypothermia have been used for selective brain cooling. Other methods for invasive cooling that are infrequently used include cold carotid infusions, single carotid artery perfusion with extracorporeal cooled blood, ice water nasal lavage, cold peritoneal and lung lavage, and nasogastric and rectal lavage.

Care of Patients Undergoing Therapeutic Hypothermia

Airway/Breathing

These comatose patients will require endotracheal intubation for airway protection, oxygenation, and ventilation control. Mechanical ventilation with 100% oxygen at a tidal volume of 10 ml/kg and a rate of 8-10 breaths/minute are initial ventilator settings that should ensure normocapnea.

The heater humidification may be turned off initially as another means of lowering patient temperature. Since the production of CO₂ is decreased by 30% when the core temperature is 33°C, the ventilator settings may need to be decreased to 6-8 breaths/minute, guided by EtCO₂ readings and ABG analysis. When ABGs are corrected for temperature, the patient appears to have a respiratory alkalosis. There is debate on whether blood gases should be corrected for temperature.²¹

Medications

Sedation is delivered to keep the patient in an obtunded, unarousable state. Medications used include propofol, fentanyl, lorazepam or midazolam. Watch for hypotension as the sedation is increased.

Paralysis to assist mechanical ventilation can be maintained by drugs such as vecuronium, cisatracurium, pancuronium, or succinylcholine. Train-of-Four stimulation should be used to monitor the patient's response level to the neuromuscular blocker, as it allows administration of the smallest dose possible to achieve the desired level of paralysis. The preferred level of blockade is 75-90%, which is 1-2 twitches following peripheral nerve stimulation.²⁴ The head of the bed should be kept at 30°, and lubricant should be provided for the eyes while receiving paralytics.

If hypotension (mean arterial pressure <70 mm Hg) persists in spite of IV fluid administration, then an inotropic drug such as dopamine, dobutamine, norepinephrine, epinephrine, or vasopressin should be infused.

Do not administer any medications labeled "do not refrigerate" to the patient. For example, mannitol may precipitate if cooled.

Cooling and Temperature Regulation

Cooling should be initiated as soon as possible even in the emergency department, using simple methods such as lowering the temperature of the room, removing clothes from the patient, turning off lights, and placing ice bags. The rapid induction of TH in many institutions is now occurring with 30 ml/kg lactated Ringers solution administered IV over 30 minutes using a high pressure bag at 300 mm Hg. The solution is kept stored in the refrigerator at 4°C. Some institutions pack the IV bag in ice to keep it cold during administration. Then a method is needed to maintain the temperature at 32-34°C; see section *Cooling Techniques*.

Core temperature should be monitored continuously and accurately. Since there is a minimal temperature gradient among brain, esophageal, and bladder temperatures, Bernard recommends that esophageal or bladder temperature be monitored.²¹ Other temperatures used include rectal, tympanic, vaginal, and pulmonary artery though rectal cannot be correlated with intracranial temperature.

Alzaga states that tympanic membrane temperature correlates well with brain temperature, is non-invasive, fast and easily applicable although the presence of auditory canal obstructions such as earwax impairs the readouts. Monitor the temperature using the tympanic method at first to make sure the patient is not warming up while waiting for insertion of a catheter to measure core temperature. Cooling of the face should be avoided in order not to decrease tympanic temperature without a corresponding decrease in brain temperature.¹⁰

During induction of TH the patient will shiver vigorously between 34°C and 35.5°C, but below this temperature the shivering stops. Shivering must be controlled, since it is associated with increased oxygen demand, acidosis and possible myocardial ischemia. Institutions report using meperidine, which reduces the shivering threshold, while causing little sedation or respiratory toxicity.

The optimal duration of TH after sudden cardiac arrest resuscitation is uncertain. The Australian study used 12 hours, while the European study used 24 hours. Bernard suggests that for patients who have significant neurologic injury, the use of TH for 24 hours seems reasonable.²¹

IV Fluids

Normal saline (NS) should be administered as the IV fluid of choice during the first 24 hours due to the presence of hyperglycemia with TH. The NS can be stopped temporarily if the CVP increases by greater than 5 mm Hg over 5 minutes. If NS or Ringers lactate are used to induce cooling, electrolytes may also need to be administered due to urinary excretion and intracellular shifts. Since potassium shifts into cells during TH, be careful with replacement especially as one approaches rewarming.

Initial Procedures

A chest radiograph should be performed during initial evaluation to exclude right main bronchus intubation and to diagnose aspiration pneumonitis and pulmonary edema. A nasogastric tube should be inserted since air often passes into the stomach during resuscitation. The insertion of an arterial line facilitates continuous blood pressure monitoring and the drawing of blood for routine laboratory tests.²¹ A 12-lead EKG can diagnose acute coronary syndromes. EKG changes that are often seen with TH include a prolonged PR and QTc, along with a J wave (called Osborne waves after the scientist who described their presence in hypothermia).²⁵ Central venous access may be required for right atrial pressure monitoring and/or inotropic medications.

Continued Monitoring

Good hemodynamic control is needed during TH. Hypothermia-induced diuresis as the patient is cooled leads to the risk of hypovolemia and hypotension. Generally more fluids are needed while the patient is hypothermic.

Good monitoring for infections is needed during TH. Evaluate for lung infections using chest x-rays and secretions since fever will not be an indication.

Finally, observe the patient's skin for any evidence of cold-related injury. Provide frequent skin care.

Physiologic Changes during Therapeutic Hypothermia

Changes that are seen during TH include:

- Hyperglycemia – use insulin to keep the blood glucose <110 mg/dl
- Decreased WBC count and function – there is an increased incidence of sepsis especially in the setting of pneumonia
- Potential decrease in amount and function of platelets, leading to prolonged clotting times – there is an increased risk of hemorrhage
- Increase in lactate level

- Mild extracellular acidosis
- Decrease in gut motility
- Urine output increases at the induction of hypothermia – so risk of hypotension – and then stabilizes when the target temperature is reached
- Decrease in heart rate
- Increase in systemic vascular resistance

Rewarming

Passive rewarming may occur by removing the source for cooling and allowing the patient to warm on his own. On the other hand, active rewarming may be programmed into the same devices as were used for cooling. Watch for afterdrop during the early stages of rewarming, which is thought due to the way heat flows through the tissues of the body. It can be avoided by heating the core organs first, as with an extracorporeal circuit. During rewarming any shivering must be suppressed with sedation. Peripheral vasodilation often occurs, and warm IV fluid may need to be given. There is some evidence that rapid rewarming may increase neurologic injury and may negate some of the protective effects of the hypothermia so aim for slow, controlled rewarming. Most institutions aim for the speed of rewarming to be 0.5-1°C/hour.

Sedation can be weaned when the patient's temperature reaches $\geq 35^{\circ}\text{C}$ and the Train-of-Four equals 4 out of 4. Wean the neuromuscular blockade when the temperature reaches $\geq 35^{\circ}\text{C}$.

Assessment of prognosis for the patient should be delayed due to the decreased rate of metabolism of drugs given during TH and rewarming. The Hospital of the University of Pennsylvania does not evaluate neurologic status and/or establish DNR status until 72 hours after ROSC.²⁶

Complications Associated with Therapeutic Hypothermia

Several studies have reported complications with the use of TH particularly at temperatures $< 32^{\circ}\text{C}$ and with an uncontrolled maintenance of temperature. Dysrhythmias, infections and primary coagulopathy are the most commonly noted complications. The HACA group reported sepsis as the main complication with TH, however this did not reach statistical significance.³

How often does unintentional overcooling occur? Merchant conducted a retrospective chart review of 32 cardiac arrest cases that had TH at two U.S. hospitals and one hospital in Europe.²⁷ Patients were excluded if temperature was not documented at least every 1-2 hours during cooling and rewarming, or if cooling was terminated prior to 18 hours. All patients received hypothermia with a cooling blanket or mattress. Temperatures $< 32^{\circ}\text{C}$ persisted for ≥ 1 hour in 20 of 32 patients (63%). Of these patients, 9 of 32 (28%) reached temperatures of $< 31^{\circ}\text{C}$. He also found that rebound hyperthermia (temperature of $> 38^{\circ}\text{C}$ at 12-18 hours after the end of active rewarming) developed in 7 of 32 patients (22%) and was treated with additional cooling.

Castro reported at the 2006 AHA Scientific Sessions that seizures are more prevalent during TH than previously thought.²⁸ Seizures have been associated to varying degrees with hypoxic encephalopathy following cardiac arrest. Twenty-eight patients who had TH with the Arctic Sun Temperature Management System had EEGs performed within 48 hours from the ROSC. Seizure activity was noted in 9 subjects (30%). Six patients were found to have EEGs consistent with status epilepticus. These seizures may contribute to poorer neurological outcome. He

concludes that performing initial EEGs in comatose cardiac arrest survivors undergoing TH may be beneficial for early detection of post-anoxic seizures.

Once the patient is cooled, s/he is usually stable. Cardiac arrest occurs infrequently during TH. If VF occurs during TH, animal studies provide us some helpful information. Boddicker used the swine model to study the affect of hypothermia on defibrillation. He induced hypothermia in swine to 33°C then placed them into VF.²⁹ After 8 minutes of VF without treatment, the swine were defibrillated using a biphasic waveform. The swine with hypothermia showed the following when compared to those who were normothermic:

- First shock success was higher (p=0.04)
- The total number of shocks needed was less (p<0.05)
- There was less refrillation (1 of 8 swine refrillated after the first minute in the hypothermic group vs 7 of 8 who were normothermic)
- The total energy delivered/animal for defibrillation was less (p=0.01)

Conclusion

Post resuscitation care is considered to be the “missing link” in the chain of survival.³⁰ Further studies are needed to determine best practice during this important time period. The low rate of TH use in the U.S is very disappointing, given the potential patient benefit. Hospitals should establish a multidisciplinary team to set up a plan for delivering TH to comatose survivors of sudden cardiac arrest. The patient’s temperature should be lowered as quickly as possible, and consideration should be given to starting the hypothermia in the emergency department. The goal is to cool to 32-34°C and maintain this temperature range for 24 hours. Several helpful websites are found in Table 2.

Table 2 Web Sites on Therapeutic Hypothermia

- <http://hypothermia.uchicago.edu/> (protocols, references, related links, slideshow)
- <http://www.med.upenn.edu/resuscitation/Hypothermia.htm> (protocols, references, books, presentations, links, discussion forum)

Research is needed to determine the optimal time to initiate TH, the speed of cooling and rewarming, and the duration of cooling. In addition, the best methods for cooling that are safe, fast and efficacious need to be studied and reported. Potential side effects need to be investigated since they have not been universally reported in research studies to date. So as you implement a TH protocol at your hospital, consider performing a research study to help answer these questions.

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