

Therapeutic Hypothermia in the Postresuscitation Patient

The Development and Implementation of an Evidence-Based Protocol for the Emergency Department

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ABSTRACT

Studies have shown that therapeutic hypothermia (TH) improves outcomes in patients who have experienced a cardiac arrest (Bernard et al., 2002; Hypothermia After Cardiac Arrest Study Group, 2002). This article discusses TH and the process used by one emergency department to develop and implement an evidence-based protocol on TH for the postresuscitation patient. **Key words:** cardiac arrest, hypothermia, induced hypothermia, therapeutic hypothermia

HERAPEUTIC HYPOTHERMIA (TH) is not a new concept. It has been trialed in patients with various diagnoses and trialed in various methods in an effort to improve patient outcomes. For the last 6-7 years, the literature has addressed using hypothermia for patients after cardiac arrest. Northwest Community Hospital (NCH) sees approximately 71,000 patients in the emergency department (ED) per year. Of these patients, approximately 12-13 patients per month arrive to the ED in cardiac arrest. It is for this population that the ED decided to review the literature and if appropriate, imple-

ical director of critical care.

ment a protocol for TH in the postresuscitated

patient. The primary sponsors of the proto-

col were the ED clinical nurse specialist and

the ED medical director. Ad hoc consultants

included ED nurses, physicians, and the med-

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HISTORY OF THERAPEUTIC HYPOTHERMIA

In 1803, Russians attempted to use hypothermia therapeutically when they covered patients with snow in an attempt to resuscitate them (Liss, 1981). In the late 1930s, hypothermia was studied in cancer patients with the hope that the decreased temperature would slow the division of cancer cells (Smith & Fay, 1940). The first study that addressed TH in cardiac arrest patients was published in 1959 (Benson, Williams, Spencer, & Yates, 1959). Unfortunately, that study and studies that followed found that patients experienced complications, such as pneumonia, bacteremia, and ventricular fibrillation from

the hypothermia. As a result, studies slowed down until approximately the 1990s. In 2003, TH received positive attention and support when the American Heart Association recommended it for patients who had a cardiac arrest (Nolan, Morley, Vanden Hoek, & Hickey, 2003). American Heart Association support of TH was based on two randomized controlled studies. One study involved patients from four hospitals in Australia, whereas the second study involved patients from five countries in Europe. In the Australian study, 49% of the patients who were treated with TH had minimal neurological impairment upon discharge from the hospital. In the normothermia group, only 26% had minimal neurological impairment (Bernard et al., 2002). In the European study, 55% of the hypothermia group had neurological outcomes that were favorable in comparison with 39% in the normothermia group (Hypothermia After Cardiac Arrest Study Group, 2002). These studies rekindled interest in the use of hypothermia for patients after a cardiac arrest.

CARDIAC ARREST

Each year, either out of hospital or in the ED, approximately 310,000 people in the United States experience sudden cardiac death (American Heart Association, 2008). An additional 375,000-750,000 people are resuscitated each year (Maramattom & Wijdicks, 2005). Approximately 40% of those resuscitated will have a return of spontaneous circulation (Maramattom & Wijdicks, 2005). Although they survive the arrest, some still have negative repercussions from the physiological responses that occur as a result of the arrest state.

When cardiac arrest occurs, there is an immediate cessation of blood flow to the brain. As a result, cerebral oxygen becomes depleted. Neurons experience lack of oxygen within the first 20 s of arrest and the central nervous system is affected within the first 5 min. Once cardiopulmonary resuscitation is initiated, only 30% of cerebral blood flow is restored (Green & Howes, 2005). Approx-

imately 30% of cardiac arrest survivors have severe brain damage (Xiao, 2002).

POSTRESUSCITATION

Immediately postresuscitation, there is an excessive increase in cerebral blood flow (Green & Howes, 2005). Following this period, for 90 min to 12 hr after the arrest, cerebral blood flow is only 50% of its baseline value, which is inadequate for cellular oxygen demands (Maramattom & Wijdicks, 2005). During this postresuscitative period, a separate chain of events occurs, even after perfusion has returned to its baseline level, which further increases tissue injury and ischemia (Holzer et al., 2005). These events include, but are not limited to, the generation of oxygen free radicals, inflammatory cell invasion, and ion imbalances (Varon & Acosta, 2008).

In postresuscitation patients, where neuronal damage has occurred, increased body temperature increases negative outcomes. In a study by Diringer, Reaven, Funk, and Uman (2004), there was a significant correlation between temperature elevation in neurology patients and poorer outcomes, higher mortality, and increased length of stay.

PHYSIOLOGY OF HYPOTHERMIA

Hypothermia counteracts some of the negative physiologic effects that occur after resuscitation. By lowering a patient's body temperature, the patient's metabolic rate is decreased. This is advantageous because it results in a decrease in oxygen demand by the cells, the same cells that are already deprived. For each 1°C decrease in body temperature, the cerebral metabolic rate is decreased by 6%-7% (Keresztes & Brick, 2006). Various studies, as cited by Smith and Bleck (2002), have shown that the negative events that occur with ischemia in the postresuscitative period (release of radicals, ion pump failure, etc.) are slowed in the presence of hypothermia. It is also believed that hypothermia, through vasoconstriction, can decrease intracranial pressure (Clifton et al., 2001).

Recognizing the effect that arrest and postresuscitation have on the neurovascular system and understanding the effect that hypothermia has on the neurovascular system, it appears reasonable that hypothermia could be advantageous in caring for the patient who has experienced cardiac arrest. These findings supported the concept of developing a TH protocol. Therefore, the literature was reviewed again for the specific information needed to develop a protocol.

LITERATURE REVIEW FOR PROTOCOL DEVELOPMENT

After scanning the literature, the ED team recognized that there were practice variations in the studies. The studies regarding TH and cardiac arrest have been very progressive; as a result, the time period in which the studies were conducted made a difference in the findings. For example, some studies used only TH when the patient's initial rhythm was ventricular fibrillation, whereas other studies included various dysrhythmias. Some studies recommended initiating TH after the return of spontaneous circulation, whereas other studies explored the option of beginning TH prior to a return of spontaneous circulation. The information that was of particular importance in developing a protocol for the ED is as follows

- Criteria for initiating TH
- Exclusion criteria
- The point in the arrest cycle to initiate TH
- The preferred method to monitor body temperature
- The target temperature range for "mild hypothermia"
- Medications to be administered
- The method of cooling that would best meet the needs of the ED by being rapid, efficient, and simple to initiate in a busy, chaotic environment.

The initial search used the keywords of "induced hypothermia" and "therapeutic hypothermia." After reviewing the literature, it was decided that only the studies from 2005 to the present, with the exception of system-

atic reviews and evidence-based guidelines, would be used. This brought the review to approximately 70 articles. After eliminating all articles that were not research articles, research-based guidelines, case studies, meta-analyses, or literature reviews, there were approximately 35 articles. The next step was to read the literature in-depth, grade it, and identify the information that was pertinent for implementing TH in the ED. The following grading scale was used:

- I: Meta-analysis
- II: Randomized controlled trials
- III: Quantitative studies
- IV: Literature reviews, research-based guidelines, and case studies

Of the 35 articles, a few were eliminated because they were repetitive reviews of the same research. Because there were enough studies with human subjects, studies that were conducted on animals were also eliminated. Of all the literature reviewed, nine were published from 2005 to 2008 and appeared to give an overall review of the findings in the literature (Table 1). Of these studies, the following facts were identified:

- the rhythm at the time of the arrest could vary rather than be limited to ventricular fibrillation;
- mild hypothermia is defined as 32-34°C and is the goal of TH;
- there were various effective methods used for cooling the patient; helmets, ice packs, cold crystalloids, cooling blankets, and combinations of the same; and
- medications would be needed to paralyze, sedate, and prevent shivering.

The nine studies included in the final literature review addressed various methods of cooling the patient and the method that immediately had an appeal was the infusion of cold crystalloids. Initiation of cold fluids would be far less difficult than cooling blankets and other methods discussed. However, because the current literature search was broad, another literature search was necessary to specifically look for information on TH and cold infusions of either lactated Ringer's

Advanced Emergency Nursing Journal

322

323

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Authors	Year	Speci Initia Year Grade rhytl	Specific Initial rhythm	Initiate TH with ROSC	Cooling Temperature method	Cooling	Method to monitor body temperature	Complicati	Complications Exclusion from TH criteria	Exclusion
Knafelj, Radsel, Ploj, & Noc (PCI patients)	2007	3	V-fib	Yes	Under 34°C	30 mJ/kg saline at 4°C over 30 min and ice packs	Bladder	Midazolam; Norcuro- nium		Profound cardiogenic shock;
										pregnancy; coagulopathy
Merchant et al.	2006	æ	V-fib; asystole; PEA	Yes	32-34°C	Mixed methods	Tympanic or bladder		Difficult to NOT overcool	
Polderman, Rijnsburger, Peerdeman, & Girbes	2005	ϵ				Refrigerated saline (4-6°C) followed by cooling blanket		Fentanyl with midazolam and/or propofol	Minimal	

Vote: TH = therapeutic hypothermia; ROSC = return of spontaneous circulation, V-fib = ventricular fibrillation; PEA = pulseless electrical activity,

or normal saline. The review was also increased to include those years back to 2002. The search yielded 10 studies specific to TH being initiated with the administration of cold fluids. However, 2 of the 10 studies were eliminated as they used animals for the study, whereas 8 studies used human subjects and therefore would provide more pertinent information (Table 2).

On the basis of the literature, the following, specific interventions were selected for the protocol. One other consideration to the development of the protocol was the standard of practice for these patients in critical care. There had to be consistency of care between the two departments.

- The contraindications in the various studies were not consistent (Table 1). Considering this and the fact that most patients did not experience negative outcomes from TH, especially when cold infusions were used (Table 2), the decision was made that the ED protocol would keep the list of contraindications to a minimum and include only those with consistency in the literature.
- Hypothermia is most beneficial when it is started within 2-6 hr after the patient arrests (Green & Howes, 2005). Cold intravenous infusions can decrease the body's temperature by 1.4°C within 30 min (Kim et al., 2005). Kliegel et al. (2007) found that by using cold infusions, patients could reach the targeted hypothermic state within 60 min. This information supports the usage of cold infusions in the ED and because of the ease may also be a future consideration for prehospital care.
- Both normal saline and lactated Ringer's were used in the studies for cold infusions (Table 2). Because the majority of the existing protocols in the ED at NCH used normal saline rather than lactated Ringer's, normal saline was chosen for the TH protocol.
- While cold infusions perform well to reach hypothermia rapidly, it is not the best choice for maintaining a hypothermic state. Although cooling blankets are

Table 2. Literature review specific to cold infusions

Author	Year	Fluid/ temperature	Amount/time to initiate TH	Method of temperature	Side effects/ comments
Bernard, Buist, Monteiro, & Smith	2003	Lactated Ringer's at 4°C	30 ml/kg over 30 min		None; Australia
Bernard & Rosalion	2008	Lactated Ringer's at 4°C			None; case study of one person; initiated before ROSC; Australia
Kim et al.	2005	0.9 normal saline at 4°C	2 L over 20-30 min	Esophageal probe	None; passive cooling measures could not sustain hypothermia; United States American Heart Association
Kliegel et al.	2007	Crystalloids at 4°C	30 ml/kg over 30 min	Bladder	None; most effective if cooled within 60 min of initiation of TH; Europe
Kliegel et al.	2005	Lactated Ringer's at 4°C	2,000 ml rapidly	Bladder	None; target body temperature achieved in <200 min from ROSC; Europe
Knafelj, Radsel, Ploj, & Noc Polderman, Rijnsburger, Peerdeman, & Girbes	2007 2005	0.9 normal saline at 4°C 0.9 normal saline at 4-6°C	30 ml/kg over 30 min 1500 ml over 30 min; if cardiogenic shock, infused over 60 min	Bladder	Increased trachea aspirates None; temperature maintained with cooling blankets; Netherlands
Virkunen, Yli-Hankala, & Silfvast	2004	Cold Ringer's	30 ml/kg at a rate of 100 ml/min	Esophageal	None; occurred prehospital; problems with esophageal temperature monitoring; Helsinki

Note: ROSC = return of spontaneous circulation, TH = therapeutic hypothermia.

Therapeutic Hypothermia in the Postresuscitation Patient

not the best method for rapidly cooling a patient, they function well in maintaining hypothermia (Kliegel et al., 2007). Using a cooling blanket to maintain the temperature is also consistent with NCH's present hypothermia protocol in critical care. Therefore, cold infusions were chosen to induce hypothermia and cooling blankets were selected to maintain hypothermia.

- Most patients that experience cardiac arrest have a urinary catheter inserted at some point during resuscitation or postresuscitation. The bladder was used in some of the studies to measure the patient's temperature (Table 2) and it is less invasive than some of the other options; for example, esophageal probe. Because of this, the TH protocol decision was to monitor temperature via a urinary catheter with a thermistor that was compatible with the existing monitoring equipment in the ED and in critical care.
- Hypothermia is an uncomfortable state and shivering may occur as a result of the low body temperature (Green & Howes, 2005). Shivering also increases the metabolic rate and generates heat; therefore, medications need to be administered to prevent shivering (neuromuscular blockers) and to minimize discomfort (sedatives).
 - Propofol and midazolam are two medications that were used frequently for sedation in hypothermic patients in the studies reviewed (Bernard et al., 2002; Bernard, Buist, Monteiro, & Smith, 2003; Hypothermia After Cardiac Arrest Study Group, 2002; Kim et al., 2005; Kliegel et al., 2007; Knafelj, Radsel, Ploj, & Noc, 2007; Polderman, Rijnsburger, Peerdeman, & Girbes, 2005). Because the NCH-ED staff was most familiar with the use of propofol for extended sedation, it was chosen for the TH protocol. Propofol is also used in the critical care protocol.
 - Vecuronium and pancuronium were

Table 3. Summary of therapeutic hypothermia protocol

Indications

Cardiac arrest with return of spontaneous circulation

Contraindications

- Pregnancy
- Pediatrics
- Trauma
- Rapidly improving neurologic deficits

Procedure

- Intubate and place on a ventilator
- Insert urinary catheter with temperature monitoring capabilities
- Obtain baseline vital signs, including a core body temperature and a neurological examination
- Monitor and document the temperature a minimum of every 15 min
- Notify critical care upon initiating the cold saline infusion.
- Begin propofol (Diprivan) at 10 mcg/kg/min intravenous infusion
- Administer Vecuronium 0.1 mg/kg bolus (maximum of 10 mg)
- Infuse 2 L of cold saline (4°C) over 30 min
- Place ice packs to the groin, both axillae, and behind the neck.
- Place the patient on a cooling blanket immediately after completion of the infusion.

used for paralysis and to prevent shivering in the literature (Bernard et al., 2002; Bernard et al., 2003; Hypothermia After Cardiac Arrest Study Group, 2002; Kim et al., 2005; Knafelj, Radsel, Ploj, & Noc, 2007). Vecuronium was chosen because it was already used in the ED and would not require additional education.

These findings and decisions were utilized to create the TH protocol for the ED. See Table 3 for a summary of the protocol.

When the patient leaves the ED for critical care, they are maintained on propofol. In

critical care, both fentanyl and cisatracurium are also administered. Train-of-four monitoring every 1 hr and as necessary is used for titration of the cisatracurium. The patient remains hypothermic for 24 hr before the rewarming process begins.

PROCESS

After determining the details for TH, the next step was to create the process for the procedure. A guiding principle used to create this process was to keep it simple and convenient. The most obvious challenge was the cold saline; how would it be kept cold, who would stock it, and how would it be billed. A refrigerator needed to be purchased that could maintain the fluids at 4°C but with the department's already limited space, the dilemma became where to keep it that would be easily accessible. For the location of the refrigerator, input was sought from the nurses. This was advantageous in not only getting their opinions and involving them but also in making them aware of TH. To check and record the temperature of the refrigerator, input was obtained from a few of the transporters; the transporters are responsible for monitoring the temperatures of all refrigerators in the department. The director of pharmacy was consulted in regards to stocking the saline.

At the end of all of these conversations, the process had been identified. The refrigerator would be located in the main room of the ED where it would be easily accessible to the staff. A new checklist was created that emphasized that the refrigerator for saline, unlike the others in the ED, needs to be maintained at a temperature of 4°C. The refrigerator is stocked with six 1-L bags of saline. Two bags of saline are located on each shelf. When the nurse needs the cold saline for a patient, it is removed from the refrigerator. Once the patient's care is complete, the nurse accesses the medication dispensing cabinet, where the bags of saline are kept, and using the patient's name, removes two bags of saline to restock the refrigerator.

EDUCATION

Char Count= 0

Once the protocol was developed and the process was created, the next step was to educate the staff. One strategy that was used to make everyone aware of the topic of TH, before the structured education began, was to set the new, empty refrigerator in the ED. It was turned on, with an external thermometer attached, to obtain the temperature of 4°C. A sign was placed on it stating, "Do not use." A new, unused, refrigerator immediately attracted attention and the ED staff began asking about it. This provided the opportunity to give short, informal in-services. They showed great interest in TH and appeared to look forward to the education and the implementation of the protocol.

Because the knowledge needs were different, although sometimes overlapping, for the various ED staff, one educational plan was created for the physicians, one for the nurses, and one for the transporters who would be responsible for checking the refrigerator. The remaining staff would become familiar with the concept through the ED newsletter. The newsletter was also used as an avenue to help with the change process. Information went into the monthly newsletter to let the staff know that TH was coming and to give updates regarding its implementation. Posters were also used to keep the staff informed.

Physicians

The ED medical director was actively involved in, and committed to, the implementation of TH. To educate the physicians, three different methods were used. The first was through informal conversations. During the development of the protocol and whenever the medical director had an opportunity to mention it, the topic of TH was discussed with the emergency physicians. This raised the interest level at an early phase.

The second method that was used for educating the physicians occurred after the protocol and process had been developed and was at an ED physician meeting. These meetings are held monthly and TH was discussed at the meeting 1 month prior to the go-live date. Both the protocol and the process were discussed. The physicians were also shown the new urinary catheters with a thermistor that would now be available in the ED. These catheters were not only to be used on TH patients but also on any other patient in whom continuous monitoring of the temperature would be advantageous.

The third method was through e-mail. Minutes from the physician's meeting were shared, via e-mail, and these minutes included the topic of TH. The medical director also e-mailed additional information regarding TH and attached two studies that discussed the advantages of TH.

In a study conducted by Merchant et al. (2006), 84% of the emergency physicians surveyed had never used hypothermia for a patient after cardiac arrest. Of these same physicians, 35% cited the reason as the procedure being technically too difficult. Because of this, it was emphasized frequently to the physicians how easy the process was and that by using the protocol with all the details of care defined, it would be even easier.

Nurses

The implementation of TH created two different educational components for the nurses; the protocol and the new urinary catheters with a thermistor. Because a new piece of equipment was involved, it was decided to provide hands-on education either individually or in small groups. It was also decided to make it convenient for the nurses and for this reason, no set education times were posted. Instead, a show on the road was offered during downtimes in the ED to review the protocol and demonstrate usage of the catheter for monitoring temperatures. Education was also offered at the beginning of each shift. This was done by having a stand, with the equipment, outside the locker room, and "catching" nurses as they exited the locker room to start their shift. The positive aspect was that some nurses heard about the in-service and

took it upon themselves to seek out an educator. Two days prior to the go-live date, all nurses, with the exception of two, had been educated to the protocol and the urinary catheter.

Transporters

Every morning, the thermometer on the refrigerator for saline must be checked and the temperature recorded on the log sheet. The primary difference between this refrigerator and the others in the ED was that the temperature was displayed and recorded in Celsius rather than Fahrenheit. A note about the new refrigerator was placed on the transporter's assignment sheet to inform them about the change. Information pertaining to the refrigerator temperature was also addressed on an individual basis with the day shift transporters.

EVALUATION

Once the protocol was developed, the next step was to monitor it for success and to see whether there was a need for revisions to the process. Within the first week of go-live, three patients had the benefit of TH. During this week, a gap in the process of replenishing the saline was also noted. Because refrigeration dates were not marked on the saline, a nurse did not know how long the saline had been in the refrigerator and theoretically, could take two bags that had just been placed in the refrigerator moments before. For this reason, the process of pulling saline from the refrigerator and restocking it was revised. The new procedure included labeling the saline bag with the date and placing the new saline bags on the bottom shelf. This also meant rotating the remaining four bags up to the top two shelves. By implementing this process, taking saline from the top shelf ensured the nurse would be obtaining the coldest bag of fluid.

Another event that required attention was the patient going to the cardiac catheterization lab (CCL) from the ED. A priority was

to prevent lengthening the time from door to balloon. To meet this expectation, it was decided that the ED staff would carry out as much of the protocol as possible without increasing the time to the CCL, and the cardiologists were comfortable with this. In a later revision, the part of the protocol that involved the cooling blanket was finessed. If time allowed, the ED would place the pads on the patient before transporting the patient to the CCL. The ED would also call critical care, who would immediately respond to the CCL with the cooling blanket.

Each month the critical care leadership and ED leadership meet to discuss any patient care issues and discuss the cases of patients who have been treated with TH. At the time of this writing, a new report has been created that identifies all patients who arrived to the ED in cardiac arrest. This report is utilized to follow-up and see how many patients receive TH and what their outcomes are. It is also helpful to audit charts of patients who do not receive TH and determine why they did not and whether there are issues that need to be addressed.

FUTURE OF THERAPEUTIC HYPOTHERMIA

At the present time, literature recommends that TH be initiated for patients who have experienced a cardiac arrest and had a return of spontaneous circulation. Studies are already showing benefit to not only beginning this procedure sooner, while the patient is still in the ambulance, but also before spontaneous circulation has returned and while cardiopulmonary resuscitation is still in progress (Bruel et al., 2008). Currently the belief is that for TH to be effective, it should be started within 6 hr of the time of arrest (Green & Howes, 2005). However, studies are being conducted at present to determine whether outcomes improve with an extended window of more than 6 hr.

Studies regarding TH are not limited to cardiac arrest. One area being explored is TH for the patient with a severe head injury (Bernard & Buist, 2003; Clifton et al., 2001).

In a study by Qiu et al. (2007), patients with a severe traumatic brain injury and a craniotomy who were maintained in a hypothermic state had better neurologic outcomes than the same type of patients who were not kept hypothermic. Both groups had complications but none related to TH. In a metaanalysis by Peterson, Carson, and Carney (2008), mortality risk and neurologic outcomes were positive when patients with traumatic brain injuries were kept hypothermic for more than 48 hr. However, there was also an increased risk of pneumonia in these same patients.

As cited by Bernard and Buist (2003), studies are also being done to see whether TH provides better outcomes in patients who have experienced traumatic cardiac arrest. Wu et al. (2008) are conducting studies on animals to determine whether hypothermia improves neurologic outcomes in cardiac arrest due to exsanguination. Other populations where TH is being explored include patients with a diagnosis of stroke, hepatic encephalopathy, bacterial meningitis, and adult respiratory distress syndrome (Bernard & Buist, 2003).

Therapeutic hypothermia is also being explored in the pediatric population. Hutchison et al. (2008) studied the effects of hypothermia on pediatric patients with severe traumatic brain injury and found no neurologic improvement. The American Heart Association recommends consideration of hypothermia in the pediatric patient who has a cardiac arrest. Many pediatric experts are calling for further research before promoting TH in the pediatric population (Hutchison, Doherty, Orlowski, & Kissoon, 2008).

Although TH is still debated in the pediatric population, it is an accepted practice in newborns with hypoxic ischemic encephalopathy. Therapeutic hypothermia has been shown to reduce mortality and neurologic deficits. Although there are shortterm adverse effects, such as thrombocytopenia, they are greatly outweighed by the positive outcomes (Jacobs, Hunt, Tarnow-Mordi, Inder, & Davis, 2007).

CONCLUSION

Therapeutic hypothermia after cardiac arrest with return of spontaneous circulation has been studied extensively throughout the world and the data demonstrate that patients experience better outcomes when it is implemented as soon as possible after arrest, that is, when the patient reaches 32–34°C within 60 min after initiating TH and stays at this temperature, without shivering, for 12–24 hr. Emergency departments have an obligation to their patients to not only initiate this procedure but also collaborate with critical care to continue the TH protocol. It is the hope of NCH that this article will assist others in meeting this goal.

REFERENCES

- Alzaga, A. G., Cerdan, M., & Varon, J. (2006). Therapeutic hypothermia. *Resuscitation*, 70, 369–380.
- American Heart Association. (2008). Sudden cardiac death. Retrieved August 14, 2008 from http://www. americanheart.org/presenter.jhtml?identifier=4741
- Arrich, J. The European Resuscitation Council Hypothermia After Cardiac Arrest Registry Study Group. (2007). Clinical application of mild therapeutic hypothermia after cardiac arrest. *Critical Care Medicine*, 35(4), 1041-1047.
- Benson, D. W., Williams, G. R., Jr., Spencer, F. C., & Yates, A. J. (1959). The use of hypothermia after cardiac arrest. Anesthesia & Analgesia, 38, 423–428.
- Bernard, S. A., & Buist, M. (2003). Induced hypothermia in critical care medicine: A review. *Critical Care Medicine*, 31(7), 2041–2051.
- Bernard, S., Buist, M., Monteiro, O., & Smith, K. (2003). Induced hypothermia using large volume, ice-cold intravenous fluid in comatose survivors of out-ofhospital cardiac arrest: A preliminary report. *Resuscitation*, 56, 9-13.
- Bernard, S. A., Gray, T. W., Buist, M. D., Jones, B. M., Silvester, W., Gutteridge, G., et al. (2002). Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *New England Journal of Medicine*, 346(8), 557-563.
- Bernard, S. A., & Rosalion, A. (2008). Therapeutic hypothermia induced during cardiopulmonary resuscitation using large-volume, ice-cold intravenous fluid. *Resuscitation*, 76, 311–313.
- Bruel, C., Parienti, J. J., Marie, W., Arrot, X., Daubin, C., Du Cheyron, D., et al. (2008). Mild hypothermia during advanced life support: A preliminary study in out-ofhospital cardiac arrest. *Critical Care*, 12(1), R31.

- Cheung, K. W., Green, R. S., & Magee, K. D. (2006). Systematic review of randomized controlled trials of therapeutic hypothermia as a neuroprotectant in post cardiac arrest patients. *Canadian Journal of Emergency Medicine*, 8(5), 329–337.
- Clifton, G. L., Miller, E. R., Choi, S. C., Levin, H. S., McCauley, S., Smith, K., et al. (2001). Lack of effect of induction of hypothermia after acute brain injury. *New England Journal of Medicine*, 344(8), 556–563.
- Diringer, M. N., Reaven, N. L., Funk, S. E., & Uman, G. C. (2004). Elevated body temperature independently contributes to increased length of stay in neurologic intensive care unit patents. *Critical Care Medicine*, 32(7), 1489-1495.
- Green, R. S., & Howes, D. (2005). Hypothermic modulation of anoxic brain injury in adult survivors of cardiac arrest: A review of the literature and an algorithm for emergency physicians. *Canadian Journal of Emergency Medicine*, 7(1), 42-47.
- Holzer, M., Bernard, S. A., Hachimi-Idrissi, S., Roine, R. O., Sterz, F., & Mullner, M. (2005). Hypothermia for neuroprotection after cardiac arrest: Systematic review and individual patient data meta-analysis. *Critical Care Medicine*, 33(2), 414–418.
- Hutchison, J. S., Doherty, D. R., Orlowski, J. P., & Kissoon, N. (2008). Hypothermia therapy for cardiac arrest in pediatric patients. *Pediatric Clinics of North America*, 55(3), 529-544.
- Hutchison, J. S., Ward, R. E., Lacroix, J., Hebert, P. C., Barnes, M. A., Bohn, D. J., et al. (2008). Hypothermia therapy after traumatic brain injury in children. *New England Journal of Medicine*, 358(23), 2447-2456.
- Hypothermia After Cardiac Arrest Study Group. (2002). Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *New England Journal of Medicine*, *346*(8), 549-556.
- Jacobs, S., Hunt, R., Tarnow-Mordi, W., Inder, T., & Davis, P. (2007). Cooling for newborns with hypoxic ischaemic encephalopathy. Cochrane Database of Systematic Reviews, 4:CD003311.
- Keresztes, P. A., & Brick, K. (2006). Therapeutic hypothermia after cardiac arrest. *Dimensions of Critical Care Nursing*, 25(2), 71–76.
- Kim, F., Olsufka, M., Carlborn, D., Deem, S., Longstreth. W. T., Hanrahan, M., et al. (2005). Pilot study of rapid infusion of 2L of 4°C normal saline for induction of mild hypothermia in hospitalized, comatose survivors of out-of-hospital cardiac arrest. *Circulation*, 112, 715-719.
- Kliegel, A., Janata, A., Wandaller, C., Uray, T., Spiel, A., Heidrun, L., et al. (2007). Cold infusions alone are effective for induction of therapeutic hypothermia but do not keep patients cool after cardiac arrest. *Resuscitation*, 73, 46–53.
- Kliegel, A., Losert, H., Sterz, F., Kliegel, M., Holzer, M., Uray, T., et al. (2005). Cold simple intravenous infusions preceding special endovascular cooling for faster

- induction of mild hypothermia after cardiac arrest-a feasibility study. *Resuscitation*, 64, 347–351.
- Knafelj, R., Radsel, P., Ploj, T., & Noc, M. (2007). Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. *Resuscitation*, 74, 227-234.
- Liss, H. P. (1981). A history of resuscitation. Annals of Emergency Medicine, 15, 65-72.
- Maramattom, B. V., & Wijdicks, E. F. M. (2005). Postresuscitation encephalopathy. Current views, management, and prognostication. *The Neurologist*, 11(4), 234-243.
- Merchant, R. M., Soar, J., Skrifvars, M. B., Silfvast, T., Edelson, D. P., Ahmad, F., et al. (2006). Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest. *Critical Care Medicine*, 34(7), 1935–1940.
- Nolan, J. P., Morley, P. T., Vanden Hoek, T. L., & Hickey, R. W. (2003). Therapeutic hypothermia after cardiac arrest: An advisory statement by the advanced life support task of the international Liaison Committee on Resuscitation. *Circulation*, 108, 118-121.
- Peterson, K., Carson, S., & Carney, N. (2008). Hypothermia treatment for traumatic brain injury: A systematic review and meta-analysis. *Journal of Neurotrauma*, 25(1), 62–71.
- Polderman, K. H., Rijnsburger, E. R., Peerdeman, S. M., & Girbes, A. R. J. (2005). Induction of hypothermia in patients with various types of neurologic injury with use of large volumes of ice-cold intravenous fluid. *Critical Care Medicine*, 33(12), 2744–2751.

- Qiu, W., Zhang, Y., Sheng, H., Zhang, J., Wang, W., Liu, W., et al. (2007). Effects of therapeutic mild hypothermia on patients with severe traumatic brain injury after craniotomy. *Journal of Critical Care*, 22, 229– 236.
- Smith, L. W., & Fay, T. (1940). Observations on human beings with cancer maintained at reduced termperatures of 75-90° Fahrenheit. *American Journal of Clinical Pathology*, 10, 1-11.
- Smith, T. L., & Bleck, T. P. (2002). Hypothermia and neurologic outcome in patients following cardiac arrest: Should we be hot to cool off our patients? *Critical Care*. 6, 377–380.
- Varon, J., & Acosta, P. (2008). Therapeutic hypothermia: Past, present, and future. Chest, 133(5), 1267-1274.
- Virkunen, I., Yli-Hankala, A., & Silfvast, T. (2004). Induction of therapeutic hypothermia after cardiac arrest in prehospital patients using ice-cold Ringer's solution: A pilot study. *Resuscitation*, 62, 299–302.
- Wu, X., Drabek, T., Tisherman, S. A., Henchir, J., Stezoski, S. W., Culver, S., et al. (2008). Emergency preservation and resuscitation with profound hypothermia, oxygen, and glucose allows reliable neurological recovery after 3 h of cardiac arrest from rapid exsanguinations in dogs. *Journal of Cerebral Blood Flow & Metabolism*, 28(2), 302-311.
- Xiao, F. (2002). Bench to bedside: Brain edema and cerebral resuscitation: The present and future. Academic Emergency Medicine, 9(9), 933-946.
- Zheng, Z, Croft, J. B., Giles, W. H, & Mensah, G. A. (2001). Sudden cardiac death in the United States, 1989 to 1998. *Circulation*, 104, 2158–2163.