Resuscitation 82 (2011) 15–20

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

A rapid, safe, and low-cost technique for the induction of mild therapeutic hypothermia in post-cardiac arrest patients☆

Pierre Kory[a,*], Justin Weiner[b], Joseph P. Mathew[a], Mayuko Fukunaga[a], Veronica Palmero[a], Bimaljeet Singh[a], Stephanie Haimowitz[c], Elana T. Clark[c], Alyssa Fischer[c], Paul H. Mayo[d]

[a] Division of Pulmonary, Critical Care, and Sleep Medicine, Beth Israel Medical Center, 7th Floor Dazian Building, New York, NY 10003, United States
[b] Internal Medicine Residency Program, Beth Israel Medical Center, 7th Floor Dazian Building, New York, NY 10003, United States
[c] Albert Einstein College of Medicine, United States
[d] Division of Pulmonary, Critical Care, and Sleep Medicine, North Shore – Long Island Jewish Medical Center, New Hyde Park, NY 11040, United States

ARTICLE INFO

Article history:
Received 30 May 2010
Received in revised form 31 July 2010
Accepted 10 August 2010

Keywords:
Hypothermia
Advanced life support (ALS)
Witnessed cardiac arrest
Post-resuscitation period
Cardiac arrest

ABSTRACT

Aim of study: The benefits of inducing mild therapeutic hypothermia (MTH) in cardiac arrest patients are well established. Timing and speed of induction have been related to improved outcomes in several animal trials and one human study. We report the results of an easily implemented, rapid, safe, and low-cost protocol for the induction of MTH.
Methods: All in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA) patients admitted to an intensive care unit meeting inclusion criteria were cooled using a combination modality of rapid, cold saline infusion (CSI), evaporative surface cooling, and ice water gastric lavage. Cooling tasks were performed with a primary emphasis on speed. The main endpoints were the time intervals between return of spontaneous circulation (ROSC), initiation of hypothermia (IH), and achievement of target temperature (TT).
Results: 65 patients underwent MTH during a 3-year period. All patients reached target temperature. Median ROSC–TT was 134 min. Median ROSC–IH was 68 min. Median IH–TT was 60 min. IH–TT cooling rate was 2.6 °C/h. Complications were similar to that of other large trials. 31% of this mixed population of IHCA and OHCA patients recovered to a Pittsburgh cerebral performance score (CPC) of 1 or 2.
Conclusion: A protocol using a combination of core and surface cooling modalities was rapid, safe, and low cost in achieving MTH. The cooling rate of 2.6 °C/h was superior to most published protocols. This method uses readily available equipment and reduces the need for costly commercial devices.

1. Introduction

The neurological and survival benefits of MTH in witnessed OHCA patients with ventricular fibrillation (VF) or ventricular tachycardia (VT) have been demonstrated in multiple randomized-controlled and historical-controlled trials over the past decade.[1–6] Consequently, the International Liaison Committee on Resuscitation and the American Heart Association recommend that comatose survivors of VF or VT after OHCA undergo MTH; and that this intervention may be beneficial in other rhythms.[7,8]

Despite these recommendations, many centers have been slow to implement cooling protocols.[9–14] A major reason cited for the lack of MTH use was the belief that using MTH is too technically difficult and slow to administer. The perceived need for a commercial device-based protocol represents a significant barrier given the costs of such devices and the limited resources of many hospitals. We report the results of a hospital-based MTH protocol that is rapid, safe, and low-cost; as it utilizes simple equipment that is readily available in hospitals.

2. Methods

Beth Israel Medical Center is an 800-bed teaching hospital in New York City. The 16 bed medical intensive care unit (MICU) is a

Abbreviations: MTH, mild therapeutic hypothermia; IHCA, in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; CSI, cold saline infusion; ROSC, return of spontaneous circulation; IH, time of initiation of hypothermia; TT, time target temperature achieved; CPC, Pittsburgh-cerebral performance score; VF, ventricular fibrillation; VT, ventricular tachycardia; MICU, medical intensive care unit.

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at doi:10.1016/j.resuscitation.2010.08.020.

* Corresponding author at: 7th Floor Dazian, 16th St. and 1st Ave, New York, NY 10003, United States. Tel.: +1 212 420 2377; fax: +1 212 420 4684.
E-mail addresses: pkory@chpnet.org (P. Kory), jiweiner@chpnet.org (J. Weiner), jmathew@chpnet.org (J.P. Mathew), mfukunag@chpnet.org (M. Fukunaga), vpalmero@chpnet.org (V. Palmero), Bimaljeet_singh@yahoo.com (B. Singh), stephhaimowitz@gmail.com (S. Haimowitz), elana.clark@gmail.com (E.T. Clark), alyssa.fischer@med.einstein.yu.edu (A. Fischer), mayosono@gmail.com (P.H. Mayo).

0300-9572/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.resuscitation.2010.08.020

Table 1
Inclusion and exclusion criteria for mild therapeutic hypothermia.

Inclusion criteria	Exclusion criteria
Return of spontaneous circulation, any arrest rhythm	Uncontrolled bleeding
No response to verbal commands	Shock state despite high dose pressors
Duration of arrest <45 min	Presence of DNR order
Any arrest location (IHCA/OHCA)	
Temperature above 34 °C	
Absence of terminal illness	
Pre-morbid independence in activities of daily living	

IHCA: in-hospital cardiac arrest; OHCA: out-of-hospital cardiac arrest; DNR: do not resuscitate.

closed book unit that is run by a full time team with approximately 1200 admissions per year. The Beth Israel Medical Center Committee for the Protection of Human Subjects approved this study.

2.1. Inclusion/exclusion criteria

Between April 2006 and April 2009, all post-cardiac arrest patients admitted to the MICU that met inclusion criteria in the absence of exclusion criteria (Table 1) were treated with MTH.

2.2. Patient evaluation and transfer

An on-call pulmonary/critical care fellow who carried a dedicated pager was responsible for rapid assessment of patients with ROSC following cardiac arrest. Patients were evaluated on the hospital wards and in the emergency department. If the patient met criteria for MTH, all emphasis was on prompt transfer to an ICU. The ICU was notified immediately of the need for MTH, so the necessary equipment could be prepared before patient arrival. The fellow initiated CSI outside of the MICU, but the other cooling modalities were applied only in the MICU.

2.3. Temperature monitoring

Rectal temperature was monitored continuously throughout MTH with a rectal temperature probe and monitor (MediThermII®, Gaymar Industries, Inc.).

2.4. Team organization and tasks

The fellow was the overall leader and used a combined teams approach. The fellow coordinated the function of three teams: floor/emergency department medical team, ICU physician team, and ICU nursing team. The ICU-based teams were given pre-printed task lists that are summarized in Table 2.

Table 2
Hypothermia preparation – team task lists.

Emergency room/medical ward team
Place two large bore peripheral IVs
Retrieve 4 L pre-cooled saline from refrigerator with 2 pressure bags
Infuse 40 ml/kg at 300 mm Hg pressure
ICU physician team
Retrieve MTH fan and bring to bedside
Fill two patient basins with room-temperature water for evaporative cooling
Fill one patient basin with ice slurry for gastric lavage
Ice orogastric tube and insert
ICU nurse team
Prepare temperature monitor with rectal probe for immediate insertion
Prepare atracurium bolus dose of 25 mg
Prepare fentanyl and midazolam infusions

MTH: mild therapeutic hypothermia.

2.5. Sedation and paralysis

All patients received midazolam (4 mg IV bolus with subsequent 2 mg/h infusion) and fentanyl (2 μg/kg IV bolus with subsequent 2 μg/kg/h infusion). All patients received a single dose of 25 mg atracurium during induction.

2.6. Cooling techniques

Induction of MTH was performed using a combination of three different techniques: (1) rapid CSI, (2) evaporative cooling by fanning the wetted, fully exposed patient, and (3) iced water gastric tube lavage. These techniques are described below. Cooling tasks were performed by a minimum of two ICU house staff physicians and one nurse. No increase in MICU nursing staff or change in MICU nurse:patient ratio was required.

2.6.1. CSI

One liter bags of 0.9% saline were pre-cooled in a refrigerator set at 4 °C. Each liter was infused as rapidly as possible under 300 mm Hg pressure (Infusable® Pressure Infusor, Vital Signs, Inc.) to a target of 40 ml/kg. Temperature, saturation, and blood pressure were assessed after each liter prior to continuing infusions. The team used the largest bore peripheral IV that was available.

2.6.2. Evaporative cooling

The patient was fully exposed and then completely wetted with a film of water using towels soaked in room-temperature water to prevent peripheral vasoconstriction. A high-speed fan (76 cm diameter Pedestal Fan Dayton Industrial Corp.) was positioned at the foot of the bed and directed over the exposed patient. The patient was re-wetted only after the majority of the skin surface became dry. This cycle of wetting and drying was repeated until target temperature was reached.

2.6.3. Ice-water gastric lavage

An orogastric tube was placed; position was confirmed via auscultation over stomach and suction of gastric fluid. Aliquots of ice water (500 ml) were injected into the tube using a 60 ml syringe. Dwell time was 5 min, followed by aspiration and instillation of a new 500 ml aliquot.

2.7. Percutaneous coronary intervention

For patients requiring coronary angiography, decisions regarding the timing and approach to MTH induction were made by the interventional cardiologist. Two techniques were adopted: (1) cooling was initiated prior to angiography using rapid CSI and a standard water-circulating cooling blanket (MediThermII®, Gaymar Industries, Inc.), with the addition of orogastric tube lavage and evaporative cooling post-procedure or (2) MTH was induced immediately upon notification using the above protocol until target temperature range was reached, followed by transfer to angiography.

2.8. Cessation of active cooling

All cooling modalities were stopped immediately upon the patient's rectal temperature reaching 34 °C.

2.9. Maintenance

Core temperature was maintained solely through the use of intermittent fanning without wetting the patient. A range of 32–34 °C was maintained for a period of 24 h. Fanning was initiated upon temperature increasing from nadir to 33.5 °C and

Table 3
Baseline patient characteristics($n = 65$).

	n (% or range)
Gender (M/F)	36 (55%) males, 29 (45%) females
Average Age	62 (28–89)
Witnessed arrest	58 (89%)
IHCA	40 (62%)
OHCA	25 (38%)
Initial rhythm VT/VF (%)	13 (20%)
Initial rhythm asystole (%)	26 (40%)
Initial rhythm PEA (%)	26 (40%)
Duration of arrest (min) (mean/range)	17 (4–60)
Starting temperature (°C) (mean/range)	36.5 (34.3–40.0)

IHCA: in-hospital cardiac arrest; OHCA: out-of-hospital cardiac arrest; VT: ventricular tachycardia; VF: ventricular fibrillation; PEA: pulseless electrical activity.

was stopped once temperature decreased to 32.5 °C. Atracurium (0.4 mg/kg bolus) was given for any episodes of shivering.

2.10. Re-warming

Following 24 h of MTH, fanning was discontinued and passive re-warming was initiated by placing a single blanket over the patient. Sedation was discontinued once the patient's temperature reached 36 °C.

2.11. Data collection

Times of notification, ROSC, IH, and TT were collected prospectively by the critical care fellow supervising the MTH protocol and entered into a spreadsheet. Data on adverse effects and outcomes were collected through a retrospective chart review. ICU nursing sheets recording hourly temperatures, vital signs, and clinical events were reviewed along with the progress notes during the MTH induction, maintenance, and re-warming phases. Neurological outcome was assessed using the Glasgow-Pittsburgh Cerebral Performance Category score (CPC) using the final documented neurological exam prior to discharge.

3. Results

A total of 65 patients received MTH. Patient characteristics are summarized in Table 3. All patients reached the target temperature range. The median ROSC–TT interval was 134 min. This interval decreased from a mean of 243 min over the first 6 months to a mean of 177 min over the final 30 months ($p = .10$). The median ROSC–IH interval was 68 min and the median IH–TT interval was 60 min. The cooling rate for the IH–TT interval was 2.6 °C/h (SD 1.6). Neurological outcomes of the patients are summarized in Table 4. Complication rates of the patients are summarized in Table 5. Complete temperature data for the induction, maintenance, and rewarming phases was available for 35 patients and is represented in Fig. 1. Three patients rewarmed to a temperature above 35 °C and required additional evaporative cooling to reduce temperature within target range. Moderate overshoot (30–31 °C) occurred in 5 patients (8%), and severe overshoot (nadir <30 °C) occurred in 5 patients (8%). No adverse effects of these temperatures were observed (e.g. arrhythmias requiring intervention, worsening hypotension, bleeding, or severe electrolyte abnormalities).

Table 4
Neurological outcomes ($n = 65$).

Location of arrest	Rhythm (n)	CPC score of 1 or 2 at discharge (n, %)
OHCA ($n = 25$)	VF/VT (8)	(2) 25%
	PEA (9)	(2) 22%
	Asystole (8)	(0) 0%
IHCA ($n = 40$)	VF/VT (5)	(3) 60%
	PEA (17)	(6) 35%
	Asystole (18)	(5) 28%

OHCA: out-of-hospital cardiac arrest; IHCA: in-hospital cardiac arrest; VF: ventricular fibrillation, PEA: pulseless electrical activity; CPC: cerebral performance category (1: conscious and alert with normal function or only slight disability, 2: conscious and alert with moderate disability, 3: conscious with severe disability, 4: comatose or persistent vegetative state, 5: brain death or death from other causes).

Table 5
Complication rates ($n = 65$).

Clinical condition	n (%)
Bleeding	7 (11)
Pneumonia	16 (25)
Sepsis	8 (12)
Acute renal failure	16 (25)
Acute renal failure requiring hemodialysis	0
Pulmonary edema	18 (28)
Arrhythmia	11 (17)
Hypotension	15 (23)

Re-warming rates were recorded for both the first 12 and 24-h periods after MTH. The faster of the two rates was used to calculate an average, maximal re-warming rate of 0.18 °C/h. Only one patient re-warmed at a rate greater than 0.5 °C/h.

4. Discussion

This study demonstrates that a protocol using rapid CSI, evaporative cooling, and ice water gastric lavage is a fast, safe, and low-cost technique for both reaching and maintaining post-cardiac arrest patients within a target temperature range of 32–34 °C for a period of 24 h. To our knowledge, this is the first report of a cooling protocol utilizing the simultaneous application of these three distinct cooling methods in post-cardiac arrest patients.

Rapid CSI is an effective and safe method for inducing MTH in post-cardiac arrest patients. There are multiple reports of its use in both pre-hospital and Emergency Department settings.[15–18] It is therefore a cornerstone of the hypothermia protocol.

Evaporative cooling by wetting a fully exposed patient with warm water under a high-speed fan is a modification of a technique used to cool heat-stroke victims on pilgrimage in Mecca, Saudi Arabia. Khogali and Weiner described body cooling units that used a high speed misting water jet for spraying hyperthermic patients while fanning them, achieving cooling rates of 3 °C/h.[19] In a variation of fanning, Israeli Defense Force soldiers have been treated for hyperthermia during desert training by being placed underneath the rotor wash of helicopters while being wetted with reported cooling rates of 8.4 °C/h.[20] We adopted fanning for MTH due to its simplicity and low-cost. The use of warm water rather than cold optimizes heat loss by preventing peripheral vasoconstriction and shivering, the body's physiologic response to prevent heat loss. Iced water gastric lavage was added as a complementary method in an attempt to optimize cooling rates, a technique used in the rapid cooling of hyperthermic patients.[21]

Our multi-modality method resulted in a cooling rate of 2.6 °C/h from IH to TT and achieved target temperature in all patients. For purposes of comparison, Table 6 lists the fastest published cooling rate for each of a variety of techniques in post-cardiac arrest patients. Our rate of cooling ranks favorably in this literature review, and was the fastest method that did not utilize a commercial hypothermia device.

The benefits of early cooling have only been demonstrated in animal models testing the effects of brief periods of therapeutic hypothermia. These studies showed that even minor temperature decreases before, during, or immediately after the time of arrest

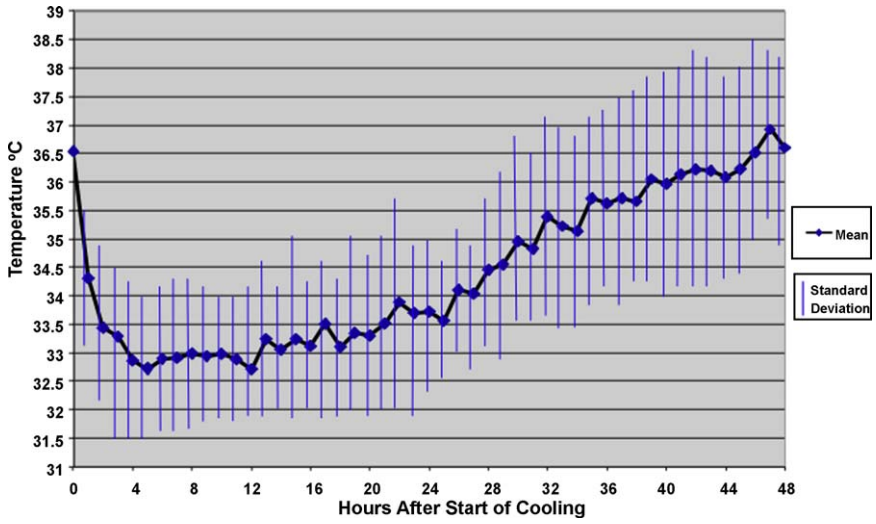

Fig. 1. Mean temperature course of MTH treated patients ($n = 35$).

were associated with benefits in neurological outcome.[35–37] Animal studies using models of prolonged hypothermia therapy have not shown a relationship between earlier cooling and outcome.[38,39] Analysis of studies in humans have shown conflicting results: a recent multivariate regression analysis of post-arrest patients found that time to coldest temperature, but not goal temperature, was the only significant independent predictor of good outcome, however, the comparison group often did not reach target within the recommended 8 h.[40] Another study analyzing a prospectively recorded registry of 986 patients after OHCA found no association between time of initiation or the time to goal temperature with neurological outcome.[41] What is agreed on is the belief that the time limit of initiation for MTH to be neuroprotective is approximately 6–8 h after return of spontaneous circulation.[42] The benefits of our rapid cooling protocol would be in helping reach target temperature well within this therapeutic window.

Time from ROSC to TT is made up of two critical intervals. The IH to TT interval depends upon the technique used to induce MTH, whereas the ROSC to IH interval is contingent upon logistical considerations, e.g. notification, transport, team organization, availability of equipment, and preparation of equipment. Over time, we worked to reduce ROSC to IH time by initiating CSI at the initial patient location without waiting for transfer to an ICU, raising clinician awareness through multi-departmental lectures, allowing earlier notification by assigning a dedicated pager, using a combined teams approach, creating unique preparation task lists for the physicians and nurses executing the cooling protocol, and widely distributing the printed protocol. With these methods, we observed a reduction in the median ROSC–IH time of 257–132 min.

The rates of complications during induction and maintenance on MTH in this study are similar to those reported in the literature for OHCA patients, despite the fact that our population included 62% of IHCA patients with significant co-morbidities.[1,2] Merchant et al. have expressed concern that overshoot below 32 °C may be associated with adverse hemodynamic and arrhythmic effects.[43] 10 patients in our study reached temperatures below 31 °C without adverse clinical consequences.

Our multi-modality MTH protocol is low-cost, using equipment that is readily available in hospitals. There are a variety of commercial devices designed primarily to induce MTH after arrest.[22–25,30] All are characterized by significant costs. A major potential barrier to implementing a post-cardiac arrest protocol relates to equip-

Table 6
Fastest reported rates of MTH induction methods in post-arrest patients.

Author, year	Method	No. of patients	IH–TT cooling rate (°C/h)
Polderman, 2005[22]	Arctic Sun® or Blanketrol II® or Cincinnati SubZero® and CSI	134	4.0[a]
Howes, 2010[23]	Thermosuit®	24	3.0[a]
Uray, 2010[24]	EmcoolsPad®	29	3.0[a]
Kory, current report	CSI and Evaporative Cooling and Gastric Lavage	65	2.6
Bruel, 2008[25]	CSI during CPR followed by ICY® Catheter	20	2.1[a]
Virkunnen, 2004[15]	CSI over 30 min	13	1.8 (target reached in 89%)
Hinchey, 2008[26]	ICY® Catheter	57	1.7[a]
Arrich, 2007[27]	*Blanket* and Ice Packs and CSI	85	1.3
Holzer, 2008[28]	Deltatherm® Air Blanket	11	1.3[a]
Haugk, 2007[29]	Arctic Sun® Pads	27	1.2[a]
Flint, 2007[30]	Innercool® Catheter and Blanketrol II® Mattress	19	1.0[a]
Gaieski, 2009[31]	Meditherm III® or ArcticSun®, CSI and Icepacks	20	1.0[a]
Bernard, 2002[2]	Ice packs	43	0.9
Oddo, 2006[6]	Ice packs and Blanketrol II®	43	0.5[a]
HACA, 2002[1]	TheraKool® mattress and ice packs	137	0.3 (target reached in 86%)
Zeiner, 2000[5]	Blanketrol II® or TheraKair mattress	27	0.3[a]
Busch, 2006[32]	Ice packs and cold towels	27	0.2 (target reached in 89%)
Don, 2009[33]	Arctic Sun® or *Blanket* and Ice packs	170	0.06[a] (target reached in 65%)
Callaway, 2002[34]	Ice Packs to Head and Neck	9	Unable to reach target

MTH: mild therapeutic hypothermia; IH: time MTH initiated; TT: time target temperature reached; CSI: cold saline infusion; CPR: cardiopulmonary resuscitation. *Blanket*: conventional water or air circulating blanket, unidentified.

[a] Uses commercial device designed for hypothermia induction.

ment acquisition cost. The MTH protocol we describe removes this obstacle.

The major strength and focus of this protocol is on the speed of the induction phase, with the maintenance phase notable for stable temperatures requiring only minimal further "active" cooling during the 24-h period. Similar low-effort maintenance phases were recently reported in the feasibility trials of the two fastest reported cooling devices, the Thermosuit® and EMCOOLSpad®.[23,24] In the Thermosuit® study, 71% of patients remained passively within range for the 24-h period after cessation of active rapid induction cooling. Similarly, in the EMCOOLSpad® study, all pads were removed once patient reached target temperature range, and 24% of patients required no further active cooling while the remainder required only intermittent additional placement of cooling pads. Although the amount of paralytics was not specifically detailed in the Thermosuit® report, continuous infusion of rocuronium was utilized in the EMCOOLSpad® protocol, thus paralytics may help explain the observed prolonged stability of temperature. In our patients, only bolus doses of atracurium were used during induction yet we observed a similar, largely passive plateau of temperatures within range, with our nurses anecdotally reporting minimal to no need for fanning within the first 12 h and only intermittently thereafter. Data on the amount of fanning required was not recorded.

Three patients re-warmed during the 24-h cooling period, and in each case the cause was attributed to a lack of familiarity with the MTH temperature maintenance protocol by the nursing staff. This emphasizes the importance of both initial and continued training of ICU staff in the MTH protocol. Our use of passive re-warming proved safe and effective, with an average maximal re-warming rate of 0.18 °C/h, slower than the maximum recommended rate of 0.5 °C/h.[44]

This report has several limitations. The results that we report are in the context of an uncontrolled trial at a single institution and may not be generalizable to other hospitals. The protocol depends on team organization and close coordination amongst different departments. Although labor-intensive, the labor is limited to a short time period, and did not require alteration in nursing ratios or staffing. Finally, rectal temperature has been shown to lag behind the core target temperature measured via an esophageal probe, which may have led to overshoot in some patients while underestimating our reported cooling rate.

5. Conclusions

Our combination cooling protocol is rapid, safe, and low cost. It can be implemented with readily available resources for successfully achieving target temperatures in post-cardiac arrest patients. A major strength of this protocol is its ability to achieve a fast cooling rate without the need for a costly commercial device.

Conflict of interest statement

No conflict of interest declared.

Acknowledgement

The authors thank Dr. Phillip Factor, Chief of the Division of Pulmonary, Critical Care, and Sleep Medicine for his assistance and support in the preparation of this manuscript.

References

1. The Hypothermia After Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurological outcome after cardiac arrest. N Engl J Med 2002;346:549–56.
2. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557–63.
3. Bernard SA, Jones BM, Horne MK. Clinical trial of induced hypothermia in comatose survivors of out-of-hospital cardiac arrest. Ann Emerg Med 1997;30:146–53.
4. Yanagawa Y, Isihara S, Norio H, et al. Preliminary clinical outcome study of mild resuscitative hypothermia after out-of-hospital cardiopulmonary arrest. Resuscitation 1998;39:61–6.
5. Zeiner A, Holzer M, Sterz F, et al. Mild resuscitative hypothermia to improve neurological outcome after cardiac arrest: a clinical feasibility trial. Stroke 2000;31:86–94.
6. Oddo M, Schaller MD, Feihl F, Ribordy V, Liaudet L. From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. Crit Care Med 2006;34:1865–73.
7. Nolan JP, Morley PT, Vanden Hoek TL, et al. Therapeutic hypothermia after cardiac arrest: an advisory statement by the advanced life support task force of the International Liaison Committee on Resuscitation. Circulation 2003;108:118–21.
8. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2005;112:IV84–8.
9. Abella BS, Rhee JW, Huang KN, Vanden Hoek TL, Becker LB. Induced hypothermia is underused after resuscitation from cardiac arrest: a current practice survey. Resuscitation 2005;64:181–6.
10. Merchant RM, Soar J, Skrifvars MB, et al. Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest. Crit Care Med 2006;34:1935–40.
11. Kennedy J, Green RS, Stenstrom R. The use of induced hypothermia after cardiac arrest: a survey of Canadian emergency physicians. CJEM 2008;10:125–30.
12. Oksanen T, Pettila V, Hynyen M, Varpula T. Therapeutic hypothermia after cardiac arrest: implementation and outcome in Finnish intensive care units. Acta Aneaesthesiol Scan 2007;51:866–71.
13. Wolfrum S, Radke PW, Pischon T, Willich SN, Schunkert H, Kurowski V. Mild therapeutic hypothermia after cardiac arrest—a nationwide survey on the implementation of ILCOR guidelines in German intensive care units. Resuscitation 2007;72:207–13.
14. Laver SR, Padkin A, Atalla A, Nolan JP. Therapeutic hypothermia after cardiac arrest: a survey of practice in intensive care units in the United Kingdom. Anaesthesia 2006;61:873–7.
15. Virkkunen I, Yli-Hankala A, Sifvast T. Induction of therapeutic hypothermia after cardiac arrest in prehospital patients using ice-cold Ringer's solution: a pilot study. Resuscitation 2004;62:299–302.
16. Bernard S, Buist A, Monteiro O, Smith K. Induced hypothermia using large volume, ice-cold intravenous fluid in comatose survivors of out-of-hospital cardiac arrest: a preliminary report. Resuscitation 2003;56:9–13.
17. Kliegel A, Janata A, Wandaller C, et al. Cold infusions alone are effective for induction of therapeutic hypothermia but do not keep patients cool after cardiac arrest. Resuscitation 2007;73:46–53.
18. Kim F, Olsufka M, Carlborn D, et al. Pilot study of rapid infusion of 2 L of 4 °C normal saline for induction of mild hypothermia in hospitalized, comatose survivors of out-of-hospital cardiac arrest. Circulation 2005;112:715–9.
19. Khogali M, Weiner JS. Heat stroke: report on 18 cases. Lancet 1980;II:276–8.
20. Hadad E, Moran DS, Epstein Y. Cooling heat stroke patients by available field measures. Intens Care Med 2004;30:338.
21. Vicario SJ, Okabajoue R, Haltom T. Rapid cooling in classic heatstroke: effect on mortality rates. Am J Emerg Med 1986;4:394.
22. Polderman KH, Rijnsurger ER, Peerdeman SM, Girbes ARJ. Induction of hypothermia in patients with various types of neurological injury with use of large volumes of ice-cold intravenous fluid. Crit Care Med 2005;33:2744–51.
23. Howes D, Ohley W, Dorian P, et al. Rapid induction of therapeutic hypothermia using convective-immersion surface cooling: safety, efficacy, and outcomes. Resuscitation 2010;81:388–92.
24. Uray T, Haugk M, Sterz F, et al. Surface cooling for rapid induction of mild hypothermia after cardiac arrest: design determines efficacy. Acad Emerg Med 2010;17:360–7.
25. Bruel C, Parienti J, Marie W, et al. Mild hypothermia during advanced life support: a preliminary study in out-of-hospital cardiac arrest. Crit Care 2008;12:R31.
26. Hinchey P, Myers B, Ho J, Lewis R, De Maio V. Time to target temperature with intravascular cooling device for survivors of out-of-hospital cardiac arrest [abstract]. Acad Emerg Med 2008;15:S91–2.
27. Arrich J, The European Resuscitation Council After Cardiac Arrest Registry Study Group. Clinical application of mild therapeutic hypothermia after cardiac arrest. Crit Care Med 2007;35:1041–7.
28. Holzer M. Devices for rapid induction of hypothermia. Eur J Anaesthesiol 2008;25:31–8.
29. Haugk M, Sterz F, Grassberger M, et al. Feasibility and efficacy of a new non-invasive surface cooling device in post-resuscitation intensive care medicine. Resuscitation 2007;75:76–81.
30. Flint AC, Hemphill JC, Bonovich DC, Therapeutic. Hypothermia after cardiac arrest: performance characteristics and safety of surface cooling with or without endovascular cooling. Neurocrit Care 2007;7:109–18.
31. Gaieski DF, Band RA, Abella BS, et al. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. Resuscitation 2009;80:418–24.

32. Busch M, Soreide E, Lossius HM, Lexow K, Dickstein K. Rapid implementation of therapeutic hypothermia in comatose out-of-hospital cardiac arrest survivors. Acta Anaesthesiol Scand 2006;50:1277–83.
33. Don CW, Longstreth WT, Maynard C, et al. Active surface cooling to induce mild therapeutic hypothermia after out-of-hospital cardiac arrest: a retrospective before-and-after comparison in a single hospital. Crit Care Med 2009;37:3062–9.
34. Callaway CW, Tadler SC, Katz LM, Lipinski CL, Brader E. Feasibility of external cranial cooling during out-of-hospital cardiac arrest. Resuscitation 2002;52:159–65.
35. Kuboyama K, Safar P, Radovsky A, Tisherman SA, Stezoski SW, Alexander H. Delay in cooling negates the beneficial effect of mild resuscitative cerebral hypothermia after cardiac arrest in dogs: a prospective, randomized study. Crit Care Med 1993;21:1348–58.
36. Hossman K. Resuscitation potentials after prolonged cerebral ischemia in cats. Crit Care Med 1988;16:964.
37. Zhao D, Abella BS, Beiser DG, et al. Intra-arrest cooling with delayed reperfusion yields higher survival than earlier normothermic resuscitation in a mouse model of cardiac arrest. Resuscitation 2008;77:242–9.
38. Colbourne F, Li H, Buchan AM. Indefatigable CA1 sector neuroprotection with mild hypothermia induced 6 hours after severe forebrain ischemia in rats. J Cereb Blood Flow Metab 1999;19:742–9.
39. Hicks SD, DeFranco DB, Callaway CW. Hypothermia during reperfusion after asphyxial cardiac arrest improves functional recovery and selectively alters stress-induced protein expression. J Cereb Blood Flow Metab 2000;20:520–30.
40. Wolff B, Machill K, Schumacher D, Schulzki I, Werner D. Early achievement of mild therapeutic hypothermia and the neurologic outcome after cardiac arrest. Int J Card 2009;133:223–8.
41. Nielsen N, Hovdenes J, Nilsson F, et al. Outcome, timing and adverse events in therapeutic hypothermia after out-of-hospital cardiac arrest. Acta Anesthesiol Scand 2009:926–34.
42. Polderman KH. Application of therapeutic hypothermia in the ICU: opportunities and pitfalls of a promising treatment modality. Part 1:Indications and evidence. Intens Care Med 2004;30:556–75.
43. Merchant R, Abella BS, Peberdy MA, et al. Therapeutic hypothermia after cardiac arrest: unintentional overcooling is common using ice packs and conventional cooling blankets. Crit Care Med 2006;34:S490–4.
44. Castren M, Silfvast T, Rubertsson S, et al. Scandinavian clinical practice guidelines for therapeutic hypothermia and post-resuscitation care after cardiac arrest. Acta Anaesthesiol Scand 2009;53:280–8.