

Should All Patients Be Treated With Hypothermia Following Cardiac Arrest?

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Summary

Cardiac arrest is a common and lethal medical problem; each year more than half a million people in the United States and Canada suffer cardiac arrest treated by emergency medical personnel or in-hospital providers. Of those who survive to hospital admission or suffer in-hospital arrest, 40–60% die prior to discharge. Neurologic injury is the major source of morbidity and mortality after recovery of spontaneous circulation. Therapeutic options to prevent neurologic injury are limited, but recent randomized trials showed that moderate therapeutic hypothermia improves neurologic outcome in selected patients following cardiac arrest. Clear consensus statements recommend that unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled if the initial rhythm was ventricular fibrillation, and that therapeutic hypothermia should be considered for other patients (other rhythms or in-hospital arrest). However, the position that all patients should be cooled following cardiac arrest is probably too broad, given the lack of studies on patients with non-ventricular-fibrillation rhythms, in-hospital arrest, or non-cardiac causes of arrest. Further research is needed to determine the broadest application of moderate therapeutic hypothermia. Key words: cardiac arrest, neurologic injury, therapeutic hypothermia, ventricular fibrillation. [Respir Care 2007;52(4):443–450. © 2007 Daedalus Enterprises]

Introduction

Cardiac arrest, both in and out of hospital, occurs commonly and results in high mortality and neurologic mor-

bidity. After initial resuscitation efforts are successful, the therapeutic options are limited, and until recently have consisted of only supportive care while awaiting recovery.

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However, experimental and recent clinical data suggest that mild therapeutic hypothermia (goal temperature 32–34°C) applied early after recovery of spontaneous circulation improves survival and neurologic function. This review discusses the potential beneficial and detrimental effects of mild therapeutic hypothermia applied after cardiac arrest.

Epidemiology of Cardiac Arrest

Out-of-Hospital Cardiac Arrest

The epidemiology of cardiac arrest is an inexact science, given that there is no national reporting mechanism, and for out-of-hospital arrest, national numbers must be extrapolated from local reports of arrests treated by the emergency medical system; the number of cardiac arrests treated by people other than emergency medical personnel is unknown. Based on data reported on emergency-medical-system-treated cardiac arrest from 35 communities in the United States, Rea et al estimated that approximately 155,000 persons experience out-of-hospital cardiac arrest each year, 60,000 (39%) of whom have ventricular fibrillation or ventricular tachycardia as the first recorded rhythm.¹ Using similar methods, Atwood et al estimated that approximately 275,000 persons suffer cardiac arrest each year in Europe, 123,000 (44%) of whom have ventricular fibrillation or ventricular tachycardia.² Median reported survival to discharge for all patients is 8.4–10.7%. Survival is somewhat better if the initial rhythm is ventricular fibrillation or ventricular tachycardia (17–21%).^{1,2}

When considering out-of-hospital cardiac arrest, it is useful to consider the fate of patients who are admitted to the hospital, given that approximately 70% die prior to admission.³ Extrapolating from the data of Rea et al and others,^{1,4} approximately 42,000 patients per year are admitted to hospital after out-of-hospital cardiac arrest, of whom approximately 19,000 (46%) survive to discharge. For patients admitted after ventricular-fibrillation/ventricular-tachycardia arrests, the likelihood of survival to discharge is slightly better (55%).

In-Hospital Cardiac Arrest

Estimates of the incidence of in-hospital cardiac arrest are similarly limited by the lack of a national reporting mechanism. It is estimated that there are approximately 0.3 cardiac arrests per licensed hospital bed per year. Given that the total number of licensed beds in the United States is approximately one million, this implies that there are about 300,000 in-hospital cardiac arrests per year. Data from the National Registry of Cardiopulmonary Resuscitation, an international registry of 375 hospitals in the United States and Canada, indicates that survival to dis-

charge after in-house arrest is approximately 18%, and approximately 36% after arrest due to ventricular fibrillation or ventricular tachycardia.⁵ The corollary to this is that the likelihood of survival after in-hospital arrest due to asystole or pulseless electrical activity is very low.

Causes of Morbidity and Mortality After Cardiac Arrest

For patients admitted after out-of-hospital cardiac arrest and for those suffering in-house arrest, anoxic brain injury and neurologic dysfunction are major sources of morbidity and mortality. Laver et al reviewed the records of patients admitted to intensive care after suffering cardiac arrest, either in or out of the hospital, over a 5-year period.⁶ Cause of death was categorized as cardiovascular, neurologic, or multiple organ failure (cardiovascular or neurologic function plus evidence of other organ-system dysfunction, infection, or systemic inflammatory response syndrome). Of 113 patients who were admitted after out-of-hospital arrest, 73% had ventricular fibrillation or ventricular tachycardia as the initial rhythm, hospital mortality was 57%, and 68% died primarily due to neurologic failure, whereas only 9% died as a result of multiple organ failure. Of 92 patients with in-hospital arrest, 35% had ventricular fibrillation or ventricular tachycardia as the initial rhythm, whereas the remainder had pulseless electrical activity or asystole. Mortality was 66%, 50% died of multiple organ failure, and 23% died of neurologic failure. Unfortunately, the number of patients who died with neurologic failure as a component of multiple organ failure was not quantified. However, it is evident from that study that neurologic failure is a major source of mortality after both out-of-hospital and in-hospital cardiac arrest.

Neurologic dysfunction also contributes to disability following discharge from the hospital after resuscitation from cardiac arrest. In the study by Laver et al,⁶ 50% of patients discharged after out-of-hospital and in-hospital arrest had some neurologic deficit.⁶ Other studies report a broad range of post-discharge neurologic dysfunction. Bunch et al reported that 88% of patients admitted after out-of-hospital ventricular-fibrillation/ventricular-tachycardia arrest were discharged with good function, and that most had a near-normal quality of life.⁷ On the other hand, in another study only 56% of the survivors of out-of-hospital cardiac arrest of noncardiac causes were discharged with good neurologic function.⁸ A report from the National Registry of Cardiopulmonary Resuscitation database of in-hospital arrests found that 73% of survivors were discharged with good neurologic function, although these data were collected from chart review rather than direct patient assessment.⁵

Table 1. Mechanisms by Which Hypothermia Prevents Brain Injury

Retards destructive enzymatic reactions
Reduces oxygen free-radical generation
Inhibits production, release, and activity of excitatory neurotransmitters
Reduces tissue oxygen consumption

In a prospective study of 231 in-hospital arrest victims in Denmark, which included a rigorous neurologic examination, only 17% of survivors were discharged with full neurologic recovery.⁹ Thus, neurologic dysfunction is a major contributor to disability in survivors of cardiac arrest.

Therapy After Initial Resuscitation: Mild Hypothermia

Beyond basic and advanced life support after return of spontaneous circulation, followed by care in the intensive care unit, there have been no specific treatments available to these patients, until recently. Given that neurologic dysfunction due to anoxic brain injury is the major source of morbidity and mortality after cardiac arrest, therapies directed toward limiting brain injury would probably improve outcomes. In this regard, mild therapeutic hypothermia (goal temperature 32–34°C) holds considerable promise.

Experimental evidence gathered over the past 2 decades supports a role for therapeutic hypothermia in limiting brain injury from diverse causes, including anoxia. Anoxia causes brain injury by multiple mechanisms, including reduction of energy stores, ion pump failure, activation of excitatory neurotransmitters, and increases in intracellular calcium.¹⁰ In addition, oxygen free-radical generation after reperfusion injures cell membranes.¹¹ Hypothermia can limit both primary (during arrest) and secondary (after recovery of circulation) brain injury, by working at several points (Table 1).^{10,12} This multi-pronged effect may explain why hypothermia is more effective than other treatments for cerebral ischemia when applied in isolation.¹³

Mild therapeutic hypothermia has been effective in reducing neurologic injury after anoxia in multiple animal species and models of ischemia, including dogs subjected to ventricular fibrillation,¹⁴ asphyxiated rats,¹⁵ and dogs with hemorrhagic cardiac arrest.¹⁶ Although therapeutic hypothermia appears to be most effective when applied prior to cardiac arrest, it is also effective when applied afterwards.^{14–16}

Three prospective randomized trials have examined the effects of mild therapeutic hypothermia after cardiac arrest. The first was a small feasibility study to determine the effectiveness of a helmet device for therapeutic cooling,

Table 2. Number-Needed-to-Treat to Save One Life in Various Conditions

Condition	Therapy	NNT
Cardiac Arrest	Hypothermia	6
ALI/ARDS	Lung-protective ventilation	11
Sepsis	Dotrecogin alpha	16
Stroke	Aspirin	33
Acute myocardial infarction	Thrombolytics	37–91*

*Depending on age
 NNT = number needed to treat (numbers derived from multiple sources)
 ALI = acute lung injury
 ARDS = acute respiratory distress syndrome

with 30 patients who had suffered out-of-hospital cardiac arrest due to pulseless electrical activity or asystole.¹⁷ Hypothermia was maintained for only 4 hours. All patients randomized to normothermia died or suffered severe disability, whereas 3 patients randomized to hypothermia survived with good performance (*n* = 2) or moderate disability (*n* = 1).

The other 2 prospective randomized trials were published simultaneously in 2002.^{18,19} Both of these trials randomized patients who had suffered out-of-hospital cardiac arrest due to ventricular fibrillation or ventricular tachycardia to either normothermia or hypothermia after recovery of spontaneous circulation. In the larger of the 2 trials, conducted in Austria, 273 patients were randomized to either normothermia or hypothermia induced with cooling blankets for 24 hours.¹⁸ A favorable neurologic outcome (survival with good performance or moderate disability) was achieved in 55% of patients randomized to hypothermia, versus 39% of those randomized to normothermia (*p* = 0.009). Six-month mortality was also lower in the hypothermia group (41% vs 55%, *p* = 0.02). The second trial was conducted in Australia, where 77 patients were randomized to normothermia versus hypothermia for 12 hours, and the hypothermia was initiated in the field with ice packs.¹⁹ Good outcome (survival with no or minimal or moderate disability) occurred in 49% of patients randomized to hypothermia, versus 26% of patients randomized to normothermia (*p* = 0.046). There was no significant difference in mortality between the 2 groups.

A meta-analysis of the above 3 studies confirmed a favorable effect for therapeutic hypothermia after cardiac arrest, with a relative risk of 1.68 (95% confidence interval 1.29–2.07) for a favorable neurologic outcome with therapeutic hypothermia.²⁰ This corresponds to a number-needed-to-treat of 6 (95% confidence interval 4–25) to prevent one unfavorable neurologic outcome. This compares favorably to the number-needed-to-treat for other common medical problems (Table 2).

Pro: Therapeutic Hypothermia Should Be Applied to All Patients Following Cardiac Arrest

The data regarding a protective effect of mild therapeutic hypothermia after out-of-hospital cardiac arrest due to ventricular fibrillation or ventricular tachycardia are consistent and convincing. The data for patients with out-of-hospital pulseless electrical activity or asystole are also consistent with a positive effect from hypothermia, although they are less robust. Given these findings, the International Liaison Committee on Resuscitation and the American Heart Association have recommended that therapeutic hypothermia be applied to all patients after recovery of spontaneous circulation after out-of-hospital ventricular-fibrillation/ventricular-tachycardia arrest, and therapeutic hypothermia should be considered for other rhythms and for in-house arrests.^{21,22} However, the International Liaison Committee on Resuscitation recommended against therapeutic hypothermia in the presence of cardiogenic shock, coagulopathy, or intractable arrhythmia.²¹ These cautions are based on the theoretical effects of hypothermia on cardiovascular function, clotting, and cardiac irritability.

Neurologic dysfunction is a major source of morbidity and mortality, independent of the cause, initial rhythm, or site of cardiac arrest; anoxic brain injury is a final common pathway following cessation of circulation. Thus, it is likely if not evident that therapeutic hypothermia will benefit patients who suffer cardiac arrest outside the narrow window of out-of-hospital ventricular fibrillation or ventricular tachycardia. Given this observation and the fact that there are no other effective treatments for resuscitated cardiac arrest victims, therapeutic hypothermia should be strongly considered for all cardiac arrest victims. In addition, therapeutic hypothermia is a low-cost treatment, compared to other therapies for critically ill patients, and can be applied virtually anywhere.

Despite strong arguments for the application of therapeutic hypothermia after cardiac arrest, the technique is underutilized. Two recent surveys of practice in the United Kingdom and North America found that a minority of centers and physicians had ever applied therapeutic hypothermia after cardiac arrest. The reasons given included insufficient evidence, lack of incorporation into advanced cardiac life support guidelines, and technical difficulties.^{23,24} The latter 2 arguments are particularly discouraging, given the considerable delay that occurs prior to incorporation of new evidence into guidelines, and the relative technical simplicity of hypothermia induction. Kim et al recently found that infusion of 2 L of 4°C saline reduces temperature to within the goal range within 30 min, and application of a cooling blanket in combination with sedation and neuromuscular blockade reliably maintains goal temperature for the duration of therapy.²⁵ The arguments

against the broad use of therapeutic hypothermia based on lack of evidence in patients with arrest due to pulseless electrical activity or asystole, or those with in-hospital arrest, are based largely on theoretical concerns that are unlikely to counteract the beneficial effects of hypothermia. Some specific examples follow.

One argument against broad application of therapeutic hypothermia is that it may have an unfavorable effect in patients with infection or septic shock; some literature suggests an immunosuppressant effect of hypothermia²⁶ and poor outcome in hypothermic patients with septic shock.²⁷ However, the data on the relationship between hypothermia and the risk of infection are inconsistent; some studies have found no relationship.²⁸ In the 2 large randomized trials of therapeutic hypothermia in survivors of cardiac arrest, hypothermia treatment was not associated with a higher risk of infection.^{18,19} Furthermore, spontaneous hypothermia during septic shock may be a marker of severity of illness rather than a causal factor in death. Compared to usual care, therapeutic hypothermia improved outcome in patients with severe septic acute respiratory distress syndrome,²⁹ and therapeutic hypothermia favorably affected outcome in experimental models of sepsis.³⁰ Also, infection is an uncommon cause of out-of-hospital cardiac arrest,^{4,31} and was present in only 27% of patients with in-hospital arrest in the National Registry of Cardiopulmonary Resuscitation database.⁵

In regard to coagulopathy, although mild hypothermia can impair blood clotting, it is not evident that this is problematic in the absence of active bleeding. There were no excess bleeding complications reported in the 2 large, randomized trials of therapeutic hypothermia after ventricular-fibrillation/ventricular-tachycardia arrest, despite the administration of thrombolytic therapy to 20% of patients in those studies.^{18,19} Thus, coagulopathy does not appear to be a compelling reason for withholding therapeutic hypothermia.

The most compelling reason for immediate and broad application of therapeutic hypothermia to cardiac arrest survivors is the potential lives saved. If all immediate survivors of out-of-hospital and in-hospital cardiac arrest, irrespective of cause, were treated with mild hypothermia, approximately 52,000 functional lives could be saved each year in the United States (using a number-needed-to-treat of 6 for functional 6-month survival, per the meta-analysis of Holzer et al) (Table 3).²⁰ If a more conservative estimate is used (upper bound of number-needed-to-treat 95% confidence interval 25, per Holzer et al), 12,600 functional lives could be saved. These data compare favorably with a potential 17,000 lives saved if another therapy, lung-protective ventilation, were uniformly applied to patients with acute lung injury and acute respiratory distress syndrome.^{32,33} Thus, although further randomized prospective trials in broader groups of patients will help further define

HYPOTHERMIA FOLLOWING CARDIAC ARREST

Table 3. Potential Impact of Broad Application of Mild Therapeutic Hypothermia

Scenario	Current Survival* (%)	Functional Lives Saved (NNT = 6)	Functional Lives Saved (NNT = 25)
Out-of-hospital ventricular fibrillation or ventricular tachycardia	55	5,000	1,200
Out-of-hospital other†	20	2,400	600
In-hospital ventricular fibrillation or ventricular tachycardia	36	11,500	2,800
In-hospital other	11	33,500	8,000
Total	–	52,400	12,600

*Survival data and numbers of lives saved are from References 1, 4, and 5.
 †“Other” refers to pulseless electrical activity, asystole, and unknown or unrecorded initial rhythm.
 NNT = number-needed-to-treat to save one functional life at 6 months after hospital discharge. NNT data from mean (6) and upper bound of 95% confidence interval (25) from Reference 20.
 NA = not available

the role of therapeutic hypothermia, awaiting those trials prior to broad application may result in considerable loss of life, particularly considering the strong conceptual rationale for its benefits in all victims of cardiac arrest.

Con: Therapeutic Hypothermia Should Not Be Applied to All Patients Following Cardiac Arrest

Though the arguments in support of therapeutic hypothermia for selected cardiac arrest victims following recovery of spontaneous circulation are compelling, the strength of evidence for applying therapeutic hypothermia to *all* patients following cardiac arrest is questionable. The specifics of the technique are variable, and there are multiple disadvantages to maintaining a critically ill patient in a cold, paralyzed, and anesthetized state for 24 hours following cardiac arrest.

In a study of patients who recovered spontaneous circulation after out-of-hospital cardiac arrest, Bernard and colleagues applied hypothermia for only 12 hours, rather than the 24 hours being debated in the present article.¹⁹ By necessity, the trial was not blinded, and death usually followed intentional withdrawal of life-sustaining measures in deeply comatose patients after 72 hours. The study was also not strictly randomized. Assignment to the treatment groups was made according to the day of the week, with hypothermia used on odd-numbered days. Patients were included only if they exhibited ventricular fibrillation at the time of arrival of the ambulance and remained in coma following recovery of spontaneous circulation. Patients were excluded if they were less than 18 years of age and male, or less than 50 years of age and female. They were also excluded from the study if they remained hypotensive (systolic blood pressure < 90 mm Hg) despite epinephrine, had other possible causes for coma, or there was no bed available in the intensive care unit of the admitting hospital. Because of these exclusions, only 77 patients were included in the data analysis, despite an enrollment period of 33 months.

The Austrian multicenter trial was limited to patients after a witnessed cardiac arrest, with a presenting rhythm of ventricular fibrillation or nonperfusing ventricular tachycardia, an interval of 5–15 min between collapse and the first attempt at resuscitation by emergency personnel, and an interval of no more than 60 min from collapse to recovery of spontaneous circulation.¹⁸ Patients were excluded if they were already hypothermic on admission, were less than 18 or more than 75 years old, if they had other possible causes of coma, if they responded to verbal commands, had persistent hypotension (mean arterial pressure < 60 mm Hg for > 30 min), were hypoxemic (arterial oxygen saturation < 85% for > 15 min), or had a known terminal condition or a known coagulopathy. Accordingly, the patient population studied was highly selected, and the enrollment period lasted nearly 5 years. In general, only 13–19% of out-of-hospital cardiac arrest patients would qualify for hypothermia treatment if that study protocol were widely applied. Indeed, only 8% of the patients who were initially assessed were included in the trial. As in the trial by Bernard and colleagues,¹⁹ the treating medical providers knew the treatment groups. Though the results nevertheless were encouraging, pneumonia, bleeding, and sepsis were more common in patients who received hypothermia. Hypothermia was maintained for 24 hours, but it may be important to note that the control group was mildly hyperthermic during the treatment period. It is unclear whether the benefit observed in that study was specifically due to hypothermia or instead to the avoidance of the hyperthermia that is quite common after recovery of spontaneous circulation. Zeiner and colleagues noted that hyperthermia after recovery of spontaneous circulation is associated with unfavorable neurologic outcomes.³⁴ In 151 patients following recovery of spontaneous circulation after witnessed cardiac arrest, they found that for each degree Celsius that body temperature was greater than 37°C, the risk of an unfavorable neurologic outcome (Cerebral Performance Category 3 or 4) increased (odds ratio 2.26, 95% confidence interval 1.24–4.12).

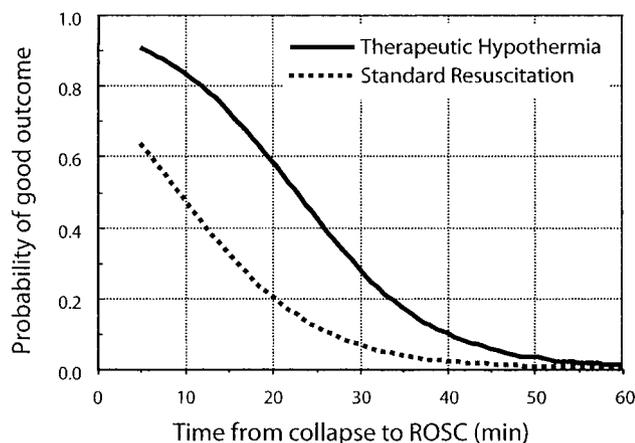


Fig. 1. Impact of therapeutic hypothermia and cardiac arrest duration on the probability of good outcome. Neurologic outcome was dichotomized as good (Glasgow-Pittsburgh Cerebral Performance category 1 or 2) or bad (category 3, 4, or 5). A duration of cardiac arrest exceeding 30 min was associated with a uniformly poor outcome, regardless of treatment. ROSC = return of spontaneous circulation. (From Reference 35, with permission)

In considering whether hypothermia should be applied following recovery of spontaneous circulation for all instances of cardiac arrest, it is important to realize that the meaningful survival rate following a non-ventricular-fibrillation/ventricular-tachycardia cardiac arrest is dismal. For example, in a randomized trial of mild hypothermia following recovery of spontaneous circulation in unconscious patients following out-of-hospital asystole or pulseless electrical activity, 87% of patients died within 2 weeks of intensive-care-unit admission.¹⁷ A retrospective single-center study by Oddo and co-workers provides additional insight.³⁵ Though they found good outcome (Cerebral Performance Category 1 or 2) in 56% of patients treated with hypothermia following resuscitation from ventricular fibrillation, mortality in patients resuscitated from rhythms other than ventricular fibrillation (asystole or pulseless electrical activity) was 87%. Therapeutic hypothermia had no benefit for those patients. The effect of hypothermia and the likelihood of a good outcome was also limited if the duration of cardiac arrest exceeded 30 min (Fig. 1).

For a novel therapy to be widely applied it should be easy to use, have clear, convincing criteria for its use, and be taught uniformly and consistently. The current techniques for therapeutic hypothermia do not fulfill those criteria. The optimal duration and depth of hypothermia remains unknown. It is possible that simply preventing fever after recovery of spontaneous circulation may be nearly as effective. The optimal method for cooling is unknown and numerous methods are available (eg, ice packs, cooling blankets, refrigerated hats, intravascular cooling catheters), some of which are aggressively marketed. Current research findings are of little help in deter-

Table 4. Disadvantages and Risks of Hypothermia

Hypothermia-induced polyuria
Electrolyte loss (K, Mg, PO ₄)
Cardiac arrhythmia
Hypovolemia
Hypotension
Hyperglycemia
Immunosuppression and increased infections
Coagulopathy

mining which method to use. With the lack of explicit protocols, uncertainty as to which patients clearly benefit, and the perception that the technique is difficult to apply, most clinicians fail to consistently use the technique.^{36,37}

Why not apply the technique to everyone after a cardiac arrest, even if there is not a clear benefit? Unfortunately, the application of hypothermia can be associated with important complications (Table 4). In surgical patients, for example, the occurrence of even mild hypothermia has been associated with significantly more postoperative wound infections.^{26,38} Hyperglycemia, which is a common complication of hypothermia, is associated with worse outcome in critically ill surgery patients.³⁹ And even if complications were trivial, it is unclear at this point whether the application of hypothermia returns patients to meaningful neurologically normal lives following cardiac arrest, since assessment of outcomes in current trials have been limited largely to gross survival and cerebral performance scores.

Summary

The evidence is compelling that moderate hypothermia is associated with better neurologic outcome in selected cardiac arrest patients. Clear consensus statements recommend that unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled if the initial rhythm was ventricular fibrillation (Table 5) and that therapeutic hypothermia should be considered for other patients (other rhythms or in-hospital arrest).^{21,22} However, the position that *all* patients should be cooled following cardiac arrest is probably too broad. Certainly, patients who quickly return to a normal mental status following defibrillation from a brief period of ventricular fibrillation need not be subjected to endotracheal intubation, sedation, paralysis, and refrigeration. Such patients can be deemed “too healthy” to benefit from hypothermia. The level of available evidence is not high enough to allow a strong recommendation for therapeutic hypothermia in patients who have been resuscitated from asystole or pulseless electrical activity, those with very prolonged resuscitation time, those with cardiac arrest from

Table 5. Summary of the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

Hypothermia Recommended

Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32–34°C for 12–24 hours if the initial rhythm was ventricular fibrillation.

Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.

Controversial Applications

Patients who remain comatose after cardiac arrest from any rhythm

In-hospital cardiac arrest

Cardiac arrest in children

Should Not Be Used Until Further Data Are Available

Severe cardiogenic shock

Life-threatening arrhythmia

Pregnant patients

Patients with primary coagulopathy

(Adapted from Reference 21)

noncardiac causes, children, and those with severe cardiogenic shock, life-threatening arrhythmia, or coagulopathy. In these cases, individual clinical discretion must be applied. Future studies may provide clarity about those patients, so that the broadest population possible can benefit from this potentially life-saving intervention.

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Discussion

Deem: I have to qualify that I wouldn't include awake patients in my all-encompassing application of hypothermia.

Pierson:* Neither of you mentioned the difficulties that you get into in monitoring patients, particularly neurologically, when they are paralyzed, sedated, and hypothermic. I wonder if anybody has any thoughts about that. I'm not so much concerned about the awake patient, although, clearly, as you've pointed out, that can be a potential problem. It's been more often a problem with patients in my care at the other extreme, where we have somebody who's been partially resuscitated from a catastrophic arrest situation, and because of a policy at our hospital that everyone gets hypothermic and paralyzed, now we have some-

one in whom all organs seem to be failing and it's obvious that the resuscitation hasn't been successful, but they can't really undergo the required testing to determine whether they are neurologically devastated.

Hurford: Yes, it delays that decision on patients who you may have decided very quickly were not salvageable. Obviously, while they are under hypothermia and paralysis, and until you're sure that all the midazolam and paralytics have gone away, you can't make a confident assessment of neurologic function. I would agree that that process sometimes prolongs the agony.

Pierson: This may not be a very powerful argument, in that the cost is merely the duration of the time that you've elected to keep them hypothermic and paralyzed, which at our hospital, by fiat, is now 24 hours on all patients.

Deem: With regard to monitoring and making decisions about end-of-life care, I think it is very unusual in

that situation to make that decision before 72 hours. Certainly, the neurologists are not going to comment on prognosis prior to that. And the other tests that we use, including SSEP [somatosensory evoked potentials] and BB bands in the cerebrospinal fluid aren't typically done until 48 hours or later. So I can't see that hypothermia would delay decisions about end-of-life care, unless you've got somebody with multiple organ failure and refractory shock, and I think you can make decisions anyway in that setting. You can use clinical judgment and stop hypothermia and evaluate neurologically, and so on.

With regard to monitoring, the other thing that has been brought up is that if you use paralysis and hypothermia, you may mask seizures, and so on. But I think the bottom line is the fact that if you use hypothermia on 6 patients, you'll save one life. And it doesn't really matter to me if I'm missing seizures in some small percentage of patients because of the paralysis and hypothermia. With regard

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to cooling patients in the field, and the potential for paralyzing patients who might wake up, I certainly wouldn't advocate that either, but I would add that we are in the process of enrolling patients into a study that will cool them in the field by administering a couple of liters of ice-cold saline. But I wouldn't advocate doing that outside the scope of a randomized prospective trial.

Hurford: I want to emphasize that your number-needed-to-treat of 6 is for witnessed arrests due to ventricular fibrillation; that number does not

apply in the very-high-mortality groups of patients found asystolic. Whether in or out of the hospital, you have to treat many more patients than 6 to see any benefit in that group.

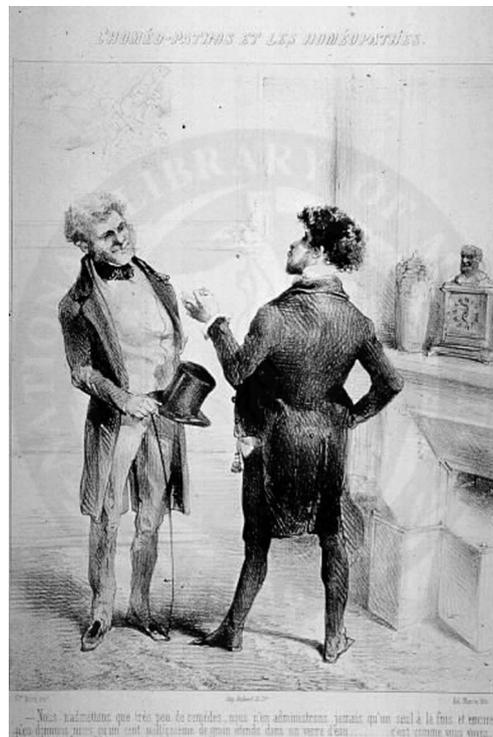
MacIntyre: Why do you have to paralyze these patients if they are comatose?

Deem: The main reason is that it is difficult to get to the goal temperature without paralysis, both because of shivering and probably because of skeletal muscle activity that you don't even see in the form of shivering. Pa-

ralysis is quite helpful in getting them to the goal temperature. Often you can stop the paralysis after you get them to the goal temperature, and they won't shiver and they'll maintain goal temperature. But for that initial induction period, paralysis is quite useful.

Hurford: Why do you have to go down to 32–34°C?

Deem: I don't know the answer to that, but that's what Safar did. There must be a biomolecular explanation, but I don't know it.



"Nous n'admettons que très peu de remèdes ..."
 Gustave Doré, inv., Edmond Morin, lith
 Paris: Aubert, 1870
 Courtesy National Library of Medicine