Therapeutic hypothermia after cardiac arrest

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Therapeutic hypothermia in selected patients surviving sudden out-of-hospital cardiac arrest can significantly improve rates of long-term survival and is considered as one of the most important clinical advancements in the science of resuscitation since 2003. The American Heart Association/International Liaison Committee on Resuscitation guidelines endorsed the use of hypothermic therapies as standard care for patients suffering from cardiac arrest while in 2005 additional inclusion and exclusion criteria were applied to patients experiencing in or out-of-hospital cardiac arrest with an initial shockable and non shockable rhythm. The goals of treatment in 2015 include achieving targeted temperature as quickly as possible with immediate initiation of cooling methods accompanied with supportive therapy and controlled rewarming.

Key words: therapeutic hypothermia, cardiac arrest, survival

INTRODUCTION

For more than a decade, mild induced hypothermia (32°C–34°C) has been standard of care for patients remaining comatose after resuscitation from out-of-hospital cardiac arrest (OHCA) with an initial shockable rhythm, and this has been extrapolated to survivors of cardiac arrest with initially non shockable rhythms and to patients with in-hospital cardiac arrest (IHCA). Targeted temperature management (TTM) previously known as therapeutic hypothermia or protective hypothermia is active treatment that tries to achieve and maintain a specific body temperature in a person for a specific duration of time in an effort to improve health outcomes. Inducing mild therapeutic hypothermia in selected patients surviving sudden OHCA can significantly improve rates of long-term neurologically intact survival and may prove to be one of the most important clinical advancements in the science of resuscitation.

EPIDEMIOLOGY

Due to its sudden and often unrecognized nature, the epidemiological characteristics are difficult to determine with precision. Nevertheless, estimates can be made.

The incidence of sudden OHCA in industrial countries is reported to be between 35.7 and 128.3 cases per 100,000, with a mean of 62 cases per year. In the US in 1998, there were 456,078 listed cases of sudden cardiac arrest. In Europe, the UK has the highest reported OHCA incidence, with 123 cases per 100,000 population per annum; this is followed by Germany with 115 cases per 100,000 population per annum. In Norway and Finland, the incidence of cardiac arrest is significantly lower with 51 and 80 cases per 100,000 population per annum, respectively.

Despite nearly 40 years of prehospital advanced life support, the survival rate of OHCA is very poor.

PATHOPHYSIOLOGY

During cardiac arrest, neurological deficits result from decreased cerebral oxygen delivery due to decreased blood pressure (BP) value and consequent lack of perfusion. Hypoxic brain state causes cerebral edema and failure of synaptic transmissions. Reperfusion can exacerbate cerebral edema, initiate destructive chemical cascades, and alter the inflammatory response with further tissue injury. The result is compromised neurological function after successful resuscitation from a cardiac event.

However, cooling the patient for 24 hours and slow rewarming, limits the effects of cerebral hypoxia and reperfusion. Hypothermia slows cerebral metabolism in terms of decrease in oxygen (O2) consumption by 6% for
each degree in body temperature reduction, limits cerebral cell death and lessens cerebral edema.\(^6\)

**HISTORY**

Hypothermia has been applied therapeutically since antiquity. The Greek physician Hippocrates, the namesake of the Hippocratic Oath, advocated the packing of wounded soldiers in snow and ice. Napoleonic surgeon, Baron Dominique Jean Larrey, recorded that officers who were kept closer to the fire, survived less often than the minimally pampered infantrymen.\(^8\)

**CLINICAL STUDIES**

In modern times the first medical article concerning hypothermia was published in 1945. This study focused on the effects of hypothermia on patients suffering from severe head injury.\(^7\)

In the 1950s hypothermia received its first medical application, being used in intracerebral aneurysm surgery to create a bloodless field. Most of the early research focused on the applications of deep hypothermia, defined as a body temperature between 20–25 °C (68–77 °F).\(^9\) Such an extreme drop in body temperature brings with it a whole host of side effects, which made the use of deep hypothermia impractical in most clinical situations. This period also saw sporadic investigation of more mild forms of hypothermia, with mild hypothermia being defined as a body temperature between 32–34°C (90–93°F).

In the 1950s, Rosomoff demonstrated in dogs the positive effects of mild hypothermia after brain ischemia and traumatic brain injury.\(^10\)

In the 1980s further animal studies indicated the ability of mild hypothermia to act as a general neuroprotectant following a blockage of blood flow to the brain. In 1999, following a skiing accident, Anna Bågenholm’s heart stopped for more than three hours and her body temperature dropped to 13.7°C (56.7°F), prior to being resuscitated.\(^11\)

Further to the animal studies and Anna Bågenholm’s accident, two landmark human studies were published simultaneously in 2002 by the New England Journal of Medicine (NEJM). One study was undertaken in 9 centers in 5 European countries, the other was conducted in 4 hospitals in Melbourne, Australia.\(^12\) Both studies, one occurring in Europe and the other in Australia, demonstrated the positive effects of mild hypothermia applied following cardiac arrest.\(^13\)

Responding to this research, in 2003 the American Heart Association (AHA) and the International Liaison Committee on Resuscitation (ILCOR) endorsed the use of targeted temperature management following cardiac arrest. Currently, a growing percentage of hospitals around the world incorporate the AHA/ILCOR guidelines and include hypothermic therapies in their standard package of care for patients suffering from cardiac arrest.\(^14\)

**CLINICAL RECOMMENDATIONS**

The 2005 AHA guidelines on therapeutic hypothermia can be summarized as follows:\(^5\):

- Unconscious adult patients with return of spontaneous circulation after OHCA should be cooled to 32-34°C for 12-24 hours when initial rhythm was ventricular fibrillation (VF) (class IIA)
- Similar therapy may be beneficial for patients with non-VF arrest out-of-hospital or with in-hospital arrest (class IIb)
- Hemodynamically stable patients with spontaneous mild hypothermia (>33°C) after resuscitation from cardiac arrest should not be actively rewarmed

**Inclusion criteria**

Patients who have been shown to benefit from induced hypothermia include the following:

- Intubated patients with treatment initiated within 6 hours after cardiac arrest (nonperfusing ventricular tachycardia (VT) or VF)
- Patients able to maintain a systolic blood pressure >90 mm Hg, with or without pressors, after cardiopulmonary resuscitation (CPR)
- Patients in a coma at the time of cooling

**Exclusion criteria**

Patients for whom hypothermia may theoretically carry increased risk include those with the following conditions:

- Recent major surgery within 14 days – possible risk for infection and bleeding
- Systemic infection/sepsis - small increase in risk of infection
- Coma from other causes (drug intoxication, preexisting coma prior to arrest)
- Known bleeding diathesis or with active ongoing bleeding - Hypothermia may impair the clotting system (however, patients may receive chemical thrombolysis, antiplatelet agents, or anticoagulants if deemed necessary in the treatment of the primary cardiac condition)
- Hypothermia is inappropriate in patients with a valid do not resuscitate order (DNR).

**TREATMENT METHODS AND PROTOCOLS**

**Cooling methods**

Cooling methods include the following:\(^7\):

- Surface cooling with ice packs
- Surface cooling with blankets or surface heat-exchange device and ice
- Surface cooling helmet
- Internal cooling methods using catheter-based technologies
- Internal cooling methods using infusion of cold fluids
**Treatment protocols**

The goals of treatment include achieving the target temperature as quickly as possible. In most cases, this can be reached within 3-4 hours of initiating cooling. Rewarming is begun 24 hours after the time of initiation of cooling.

**External cooling with cooling blankets or surface heat-exchange device and ice**

Before initiating cooling, confirm eligibility and gather materials.

- Obtain 2 cooling blankets and cables (one machine) to “sandwich” the patient; each blanket should have a sheet covering it to protect the patient’s skin
- Alternatively, place heat-exchange pads on the patient per the manufacturer’s recommendation
- Pack the patient in ice (groin, chest, axillae, and sides of neck); use additional measures as needed to bring the patient to a temperature between 32°C and 34°C; avoid packing ice on top of the chest, which may impair chest wall motion
- Monitor vital signs and oxygen saturation and place the patient on a continuous cardiac monitor, with particular attention to arrhythmia detection and hypotension
- Once a temperature below 34°C is reached, remove ice bags and use the cooling blanket or heat-exchange device to maintain temperature between 32°C and 34°C

**Supportive therapy**

- A mean arterial pressure (MAP) goal of more than 80 mm Hg is preferred; hypertension is potentially additive to the neuroprotection of hypothermia
- Norepinephrine can be used, starting at 0.01 mcg/kg/min and titrated to a MAP > 80 mm Hg
- Practice standard neuroprotective strategies such as placing the head of the bed at 30°
- Monitor for arrhythmia (most commonly bradycardia) associated with hypothermia
- If life-threatening dysrhythmia arises and persists, or hemodynamic instability or bleeding develops, discontinue active cooling and rewarm the patient
- During cooling, an ECG Osbourne or camel wave may be present; heart rate less than 40 bpm is common and is not a cause for concern in the absence of other evidence of hemodynamic instability
- Check skin every 2-6 hours for thermal injury caused by cold blankets
- Regularly check the patient’s temperature with a secondary temperature monitoring device when cooling
- Do not provide nutrition to the patient during the initiation, maintenance, or rewarming phases of the therapy

**Controlled rewarming**

Begin rewarming of the patient 24 hours after the initiation of cooling.

- Rewarm slowly at a rate of 0.3-0.5°C every hour
- Rewarming will take approximately 8 hours
- Remove cooling blankets (and ice if still in use)
- One method is to set the water temperature in the cooling device to 35°C and then increase the water temperature by 0.5°C every 1-2 hours until a stable core body temperature of 36°C has been reached for 1 hour
- Maintain the paralytic agent and sedation until the patient’s temperature reaches 35°C; if infusing, discontinue the paralytic agent first; the sedation may be discontinued at the practitioner’s discretion
- Monitor the patient for hypotension secondary to vasodilation related to rewarming
- Discontinue potassium infusions
- Avoid hyperthermia

**DISCUSSION**

Similar treatment recommendations were provided in the “2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations”.

A 2011 meta-analysis of randomized controlled trials found that therapeutic hypothermia with conventional cooling methods improves both survival and neurologic outcomes at hospital discharge for patients who experienced cardiac arrest.

An international, multicenter, randomized trial published in NEJM in 2013, compared a target body temperature of 33°C with one of 36°C in patients who had been resuscitated after out-of-hospital cardiac arrest of presumed cardiac cause. Results reported no significant differences between the two groups in overall mortality at the end of the trial or in the composite of poor neurologic function or death at 180 days. On the basis of these results, decisions about which temperature to target after out-of-hospital cardiac arrest require careful consideration.

After publication of the seminal trials of therapeutic hypothermia after cardiac arrest, this approach was recommended in international guidelines, despite arguments by some investigators that the evidence was weak, owing to the risk of bias and small samples.

**CONCLUSION**

Highlights from the 2015 Recommendations for Post-Cardiac Arrest Care from the American Heart Association include:

1. Class I (strong) recommendations for:
   a. TTM to treat comatose post-cardiac arrest patients suffering out-of-hospital VF/pulseless VT (LOE B-Randomized)
   b. TTM to treat comatose post-cardiac arrest patients suffering non-VF/pulseless VT (‘non-shockable’) rhythms and IHCA (stronger recommendation than the 2010 guidelines) (LOE C-Expert Opinion)
   c. Selection and maintenance of a constant temperature within the range 320C and 360C (LOE B-Randomized)
TARGETED TEMPERATURE MANAGEMENT

A. Iglica et al.

ACI Vol. LXIII

SUMMARY

TERAPEUTSKA HIPOTERMIIJA NAKON SRČANOG ZASTOJA

Terapeutksa hipotermija sprovedena kod odabranih pacijenata koji prežive iznenadni nastup vanboličkog srčanog zastoja može značajno poboljšati stopu dugoročnog preživljavanja i smatra se jednom od najznacajnijih napredaka kliničke prakse u sprovedenju reanimacijskog postupka. Od 2003. godine vodič Ame-
ričkog udruženja za srce te Internacionalnog (Liaison) komiteta za oživljavanje potvrdili su upotrebu terape-
utske hipotermije kao standarda medicinske njege za pa-
cijente koji su doživjeli srčani zastoj dok su u 2005.
dodatni kriteriji uključenja i isključenja primijenjeni na
pacijente koji su doživjeli vanbolički nastup srčanog
zastoja sa inicijalnim soknim i nesoknim srčanim ritmom.
Cilij tretmana u 2015. uključuje postizanje ciljne tjelesne
temperature, što je prije moguće, sa trenutnim zapo-
čanjem metoda hlađenja praćenih suportivnom terapijom
i kontroliranim ponovnim zagrijavanjem.

Ključne reči: terapeutksa hipotermija, srčani zastoj,
preživljavanje.

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