THERAPEUTIC HYPOTHERMIA

SUMMARY

Therapeutic hypothermia by conventional cooling methods after cardiac arrest has been shown to attenuate neurologic damage and improve survival. Standard therapeutic hypothermia consists of cooling the patient to 32-34°C for 24 hours. Although many trauma patients who develop cardiac arrest may not be candidates for therapeutic hypothermia due to the risk of either worsening or contributing to coagulopathy, it should be considered in patients without significant contraindication.

RECOMMENDATIONS

- **Level 1**
  - **Comatose adult patients with out-of-hospital ventricular fibrillation or ventricular tachyarrhythmia cardiac arrest, and a presumed cardiac cause of the arrest, should be cooled to 33°C for 24 hours.**
- **Level 2**
  - **Comatose adult patients with an out-of-hospital asystolic cardiac arrest should be cooled to 33°C for 24 hours.**
  - **Comatose adult patients with an out-of-hospital cardiac arrest not from a presumed cardiac cause should be cooled to 33°C for 24 hours.**
- **Level 3**
  - **Comatose adult patients with an out-of-hospital cardiac arrest from asphyxiation should be cooled to 33°C for 24 hours.**
  - **Comatose adult patients with an in-hospital cardiac arrest should be cooled to 33°C for 24 hours.**
  - **In patients where cooling to 33°C is contraindicated, consider cooling to 36°C for 24 hours.**

INTRODUCTION

Out-of-hospital cardiac arrest is associated with poor survival and poor neurological outcomes. Cerebral reperfusion results in the generation of free radicals and other mediators that trigger chemical cascades resulting in further damage to the brain. Therapeutic hypothermia acts via multiple pathways to reduce brain cell death, including inhibiting the release and uptake of glutamate and dopamine, preservation of the blood brain barrier, continuation of ATP stores, and restitution of the microcirculation (1).

Therapeutic hypothermia is a relatively recent concept with many details still to be determined. Although there is relatively good evidence of benefit in comatose patients with an out-of-hospital ventricular fibrillation or tachyarrhythmia from a cardiac cause, there is limited data regarding other initial rhythms and non-cardiac causes of arrest. Additionally, there are limited studies regarding the temperature and duration for therapeutic hypothermia. The current American Heart Association guidelines are as follows:

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

> "We recommend selecting and maintaining a constant target temperature between 32°C and 36°C for those patients in whom temperature control is used (*strong recommendation, moderate-quality evidence*). Whether certain subpopulations of cardiac arrest patients may benefit from lower (32°C–34°C) or higher (36°C) temperatures remains unknown, and further research may help elucidate this. We recommend Targeted Temperature Management (TTM) as opposed to no TTM for adults with out-of-hospital cardiac arrest (OHCA) with an initial shockable rhythm who remain unresponsive after return of spontaneous circulation (ROSC) (*strong recommendation, low-quality evidence*). We suggest TTM as opposed to no TTM for adults with OHCA with an initial non-shockable rhythm who remain unresponsive after ROSC (*weak recommendation, very-low-quality evidence*). We suggest TTM as opposed to no TTM for adults with in-hospital cardiac arrest (IHCA) with any initial rhythm who remain unresponsive after ROSC (*weak recommendation, very-low-quality evidence*). In making these recommendations, we place a higher value on the potential for increased survival with good neurologic outcome as compared with the possible risks (which appear to be minimal) and the cost of TTM. We emphasize that the mortality after cardiac arrest is high and the treatment options are limited. Although the evidence for TTM compared with no temperature management is of low quality, it is the only post-ROSC intervention that has been found to improve survival with good neurologic outcome. We have, therefore, made our recommendation strong in spite of the low-quality evidence." (2)

In the trauma population, therapeutic hypothermia may be limited due to concerns for either worsening or contributing to coagulopathy. However, it does have a potential role in patients with cardiac arrest due to asphyxia without other associated injuries.

LITERATURE REVIEW

Bernard et al. performed a randomized, controlled trial to compare moderate hypothermia to normothermia after out-of-hospital cardiac arrest. All patients had ventricular fibrillation as the first recorded rhythm and remained comatose after return of spontaneous circulation. Hypothermia was initiated in the field by application of cold packs and furthered upon arrival. Patients randomized to hypothermia were maintained at 33°C for 12 hours. At 18 hours, patients were actively rewarmed over 6 hours. Patients randomized to normothermia were maintained at 37°C. 77 patients were included in the study; 43 were treated with hypothermia. 49% of patients treated with hypothermia had a good outcome, defined as discharge to home or rehabilitation, compared to 26% of normothermic patients, resulting in an odds ratio for good outcome with hypothermia of 5.25. There was no reported difference in adverse effects (3).

The Hypothermia after Cardiac Arrest Study Group performed a multicenter, randomized, controlled trial to compare moderate hypothermia to normothermia after out-of-hospital cardiac arrest. All patients had ventricular fibrillation or nonperfusing ventricular tachycardia as the first recorded rhythm. Hypothermia was initiated upon hospital arrival with an external cooling device to a target temperature of 32 to 34°C, which was maintained for 24 hours, followed by passive rewarming. Patients randomized to normothermia were maintained at 37°C. 273 patients were included in the study; 136 were treated with hypothermia. 55% of patients treated with hypothermia had a good outcome, defined as Pittsburgh cerebral-performance category of 1 (good recovery) or 2 (moderate disability), compared to 39% of normothermic patients, resulting in a risk ratio of 1.4. Six-month mortality was 42% in the hypothermia group and 55% in the normothermia group, resulting in a risk ratio of 0.74. There was no reported difference in adverse effects (4).

A 2012 Cochrane Review of pooled data from the studies above, as well as an abstract and a feasibility study concluded that therapeutic hypothermia is beneficial in patients with out-of-hospital cardiac arrest, a presumed cardiac cause of arrest, and ventricular fibrillation or ventricular tachycardia as the first recorded arrhythmia (5-7). However, the sample size for asystole and non-cardiac causes of arrest were too small to draw significant conclusions.

Nielsen et al. performed a multicenter, randomized, controlled trial to compare hypothermia at 33-36°C (8). All patients had a GCS less than 8 and a first recorded rhythm other than asystole. Hypothermia was initiated after hospital arrival using a combination of external and intravascular cooling devices at the preference of the center and maintained for 28 hours, followed by rewarming at 0.5°C hourly. Evaluation at 180 days revealed no statistically significant difference in mortality or neurological outcome between the groups. A serious adverse event, such as seizure, infection, bleeding, cardiac arrhythmia, or electrolyte deficit, occurred in 93% of patients cooled to 33°C, compared to 90% of those cooled to 36°C, which was a statistically significant difference.

A 2016 Cochrane Review update that included the above study, as well as a study looking at hypothermia in conjunction with hemofiltration, found that recent studies did not provide additional data that required altering the conclusions of the 2012 review (9).

Baldursdottir et al. published a case series evaluating neurological recovery for all forms of asphyxiation. The case series looked at 14 patients treated with therapeutic hypothermia. Nine patients had a cardiac arrest, and all were comatose with a GCS of 3-5. Nine of fourteen survived with minimal neurological impairment. Of the five non-survivors, four had cerebral edema on the initial CT scan (10).

Targeted Temperature Management Checklist

- ☐ Admit to ICU
- ☐ Place patient on continuous pulse oximetry, telemetry, and EEG monitoring
- ☐ Initial labs: CBC, PT/INR, PTT, CMP, magnesium, phosphorus, ionized calcium, cortisol, lactate, ABG
- ☐ Maintain patient NPO
- ☐ Heparin for DVT prophylaxis
- ☐ Pepcid for GI prophylaxis
- ☐ Standard glucose management
- ☐ Apply Lacri-Lube to both eyes and cover with pads
- ☐ Apply the Bard® Arctic Sun in automatic mode with a target temperature of 33°C
    - Temperature should be taken with a rectal, esophageal, or bladder temperature probe
        - A bladder temperature probe should not be used in anuric patients
    - Target temperature should be reached within 1 hour
    - Monitor temperature hourly
- ☐ A heated humidification ventilator circuit should be set to 34°C
- ☐ Sedation should be maintained for a RASS of <1
- ☐ If the patient starts shivering, start fentanyl and versed drips for a RASS of -5 and initiate rocuronium for paralysis
    - Bolus rocuronium 50 mg IV initially and then start a drip titrated so that the patient does not shiver until 33°C is reached. Then stop the drip and bolus 50 mg as needed to prevent shivering.
- ☐ Serial labs every 6 hours:
    - K, Mg, iCa, Phos, ABG
    - Do not use standard electrolyte replacement protocols
        - Give 40 mEq KCl for K <3.4
        - Give 1 gm Mg for Mg <1.8
        - Give 1 gm CaCl for iCa < 0.9, check iCa Q4 while replacing
        - Give 10mMol NaPh for Ph < 2.5
- ☐ Start rewarming 24 hours after the initiation of hypothermia
    - Rewarm at 0.25°C to a target temperature of 37°C
- ☐ Wean off sedation after rewarming is complete

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