Hypothermia: Hospital Protocols and Potential Complications

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Studies

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INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST

Mild hypothermia induced by a helmet device: a clinical feasibility study

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Hypothermic

Normothermic

Alive at 6 months

with favorable neurologic status

53% (75/136)

35% (54/137)
ILCOR Advisory Statement

Therapeutic Hypothermia After Cardiac Arrest
An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

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• Unconscious adult patients with ROSC after out-of-hospital VF cardiac arrest should be cooled to 32°C - 34°C for 12 - 24 hours

• Possible benefit for other rhythms or in-hospital cardiac arrest
Cooling Technique

- Cooling blankets: 50%
- Ice / cold liquid packing: 15%
- Ice / cold liquid gastric lavage: 13%
- IV cooling catheter: 2%
- Cooling mist: 2%
- Other method: 17%
Technology

- Novel coolant fluids
- Cold IV fluids
- Cooling catheters
POST RESUSCITATION SUPPORT

ROSC – RETURN OF SPONTANEOUS CIRCULATION

Airway & Breathing
Airway- Maintain and protect airway
Admin 100% Oxygen
Breathing – DO NOT HYPERVENTILATE
Maintain respiratory rate of 10-12 min
Monitor ETC02 / SP02

CIRCULATION
Treat hypotension < 90mmhg
• Consider fluid bolus
• Dopamine 5-20ug/kg IV/IO
• Obtain a 12-Lead EKG – STEMI cases to PCI capable facilities

Cardiac Arrest from any medical etiology
And patient is unresponsive
and hemodynamically stable

Initiate Therapeutic Hypothermia
• Apply ice packs to axilla / chest/ groin
• Administer cold IV fluids 30ml/kg @ 500cc increments
• Monitor temperature
• Treat shivering with Ativan 2.0-4.0 mg
Vecuronium 0.1 mg/kg IV/IO

Transport to THP capable facility
Notify ED to prepare for continuous Cooling.
# Summary of Landmark Trials

<table>
<thead>
<tr>
<th></th>
<th>HACA (European)</th>
<th>Bernard (Australian)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial rhythm</td>
<td>VF or VT</td>
<td>VF</td>
</tr>
<tr>
<td>Pre ED Cooling</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Target Temp</td>
<td>32 to 33 C</td>
<td>33 C</td>
</tr>
<tr>
<td>Hypothermia patients</td>
<td>136</td>
<td>43</td>
</tr>
<tr>
<td>Standard Rx Patients</td>
<td>137</td>
<td>34</td>
</tr>
<tr>
<td>Hypothermia duration</td>
<td>24 hours</td>
<td>12 hours</td>
</tr>
<tr>
<td>Morbidity Reduction</td>
<td>ARR 16%, NNT 6</td>
<td>ARR 16%, NNT 4</td>
</tr>
<tr>
<td>Mortality Reduction</td>
<td>ARR 14%, NNT 6</td>
<td>ARR 17%, NNT 6</td>
</tr>
<tr>
<td>Adverse events (sepsis, arrhythmias &amp; Bleeding)</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Who to Cool?

Inclusion Criteria

• Post-cardiac arrest: defined as absence of pulses requiring chest compressions, regardless of location or presenting rhythm

• Any Initial rhythm (VF/VT, asystole or PEA)

• ROSC within 60 minutes to a SBP > 90 mmHg (with or without vasoactive meds)—ClassI LOE: B (AHA Guidelines for CPR)

• Patient is comatose (unable to follow commands/ GCS < 6) upon arrival to the hospital in the absence of sedation

• Time at start of cooling is within 4 hours after ROSC
Who to Cool?
Exclusion Criteria

• Another reason to be comatose
• Hemorrhagic stroke

• Purposeful response to verbal commands or noxious stimuli after ROSC and prior to initiation of hypothermia

• Absent brainstem function not explained by treatment with sedatives, paralytics or anti-cholinergic agents

• A known terminal illness preceding arrest

• ? Pregnancy (Case report showing benefit)
Who to Cool?
Exclusion Criteria

- Pre-existing DNR and / or DNI code status and patient not intubated as part of resuscitation efforts

- **Multi-organ system failure**, refractory shock requiring high doses of vasopressors (MAP<60 on 2 or more vasopressor agents), severe persistent hypoxia, acidosis or co-morbidities with minimal chance of meaningful survival independent of neurological status

- Uncontrolled bleeding to coagulopathy

- Recurrent VF or refractory VT in spite of appropriate therapy should generate consideration of emergent referral for cardiac catheterization
Absolute Contraindications

- Hemorrhagic stroke
- Cardiac arrest due to trauma
- GCS > 8 on arrival of EMS
- Pre-existing hypothermia (<34 C; 93.2F)
- Uncontrolled, active bleeding
- Uncontrolled hemodynamically unstable rhythms
Relative Contra-indications

- Prolonged cardiac arrest (>60 minutes)
- Refractory hypotension despite fluid and vasopressor support
- Thrombocytopenia (plt<50K) or baseline coagulopathy
- Pregnancy (? –one positive case report)
- Terminal condition or poor baseline status (unable to carry out simple ADL’s)
“Gray” Areas

- Witnessed in-hospital arrest with VF/VT
- Out-of-hospital cardiac arrest with initial PEA or asystole
“Mild” Hypothermia

• In-hospital post-arrest pts with any initial rhythm
• Out-of-hospital arrest with rhythms othr than VT/VF

Very little data
2010 AHA CPR Guidelines give this a Class IIb LOE:B
*There is also little known about use of “mild hypothermia” in post-arrest pts in circulatory shock requiring vasopressors or IABP
Coronary Angiography

- 84 consecutive survivors of out-of-hospital cardiac arrest
  - 36 had ST-elevation
  - Cor angio found acute coronary occlusion in 40 of the 84 (ST-elevation was a strong predictor) $p=0.004$
  - 9 pts without chest pain or ST elevation were found to have occluded infarct related artery
  - Successful angioplasty was an independent predictor of survival

Spaulding, et al. NEJM1997; 336:1629-1633
Parisian Region Out of Hospital Cardiac Arrest Trial
Circ Cardiovasc Interv 2010:3:200-207

• Registry of 435 patients who had no obvious extra-cardiac cause of arrest
• Successful culprit coronary angioplasty was associated with survival
• “Mild” hypothermia employed prior to and on arrival to lab

Wolfrum. Crit Care Med 2008; 36;1780-1786
Typical Cooling and Rewarming Protocol

- **Cooling (8-12 hr)**
- **Cold (12 hr)**
- **Rewarming (24 hr)**

Bladder temperature [°C]

Time after Restoration of Spontaneous Circulation (hours)
How to Cool?

ICU Notification

- Once eligibility for induced hypothermia is determined, call MICU/Stroke attending ASAP

- Obtain 2 large bore IV lines

- Obtain baseline temperature

- Infusion of **approximately 2 to 3 liters** (for 70 kg individual) of normal saline refrigerated at 4-5 °C
  - Can safely and reliably lower core body temperature by 3-4 °C when infused over 50 minutes.
How soon?

• Randomized trial of 2,334 survivors of out-of-hospital cardiac arrest
  – No better if hypothermia started by paramedics than if it was started on arrival at the hospital 47.5% vs 52.6% discharged to home or rehabilitation  p=0.43
  Bernard. Circ 2010;122:737-742

• Therefore, start as soon as possible after a comprehensive clinical evaluation

COOLING PROTOCOL

- Obtain laboratory tests ASAP:
  - Beta HCG on all women of childbearing age
  - Arterial blood gas
  - CBC/ platelets / PT / PTT/INR, Fibrinogen
  - Electrolyte “panel 7”, plus iCa / Mg / Phos , Cl-, Glucose
  - Amylase, Lipase, LFTs, , Lactate, CPK-MB, CK, Troponin
  - Blood Cultures, Urine Cultures, Urinalysis

- Toxicology screen if appropriate

- 12 lead EKG, Chest X-ray

- Placement of urinary catheter with temperature sensor

- Insertion of Central Line Catheter (subclavian or IJ)
<table>
<thead>
<tr>
<th>TIME</th>
<th>TASK</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIME ZERO</td>
<td>RETURN OF SPONTANEOUS CIRCULATION (ROSC)</td>
</tr>
<tr>
<td>10 MINUTES</td>
<td>COMPLETE SCREENING &amp; NOTIFY ICU ATTENDING</td>
</tr>
<tr>
<td>15 MINUTES</td>
<td>• “HYPOTHERMIA LABS” TO BE SENT OUT</td>
</tr>
<tr>
<td></td>
<td>• START COLD SALINE</td>
</tr>
<tr>
<td>30 MINUTES</td>
<td>PLACE CENTRAL LINE IN SUBCLAVIAN</td>
</tr>
<tr>
<td></td>
<td>PLACE TEMP SENSING FOLEY</td>
</tr>
<tr>
<td>45 MINUTES</td>
<td>START SURFACE COOLING</td>
</tr>
<tr>
<td>4 HOURS</td>
<td>ACHIEVE TARGET TEMP OF 32 C</td>
</tr>
</tbody>
</table>
METHODS

• Ice packs head, groin, and axillae
• Intravenous infusion of saline maintained at 4C/39F
• Cooling air blankets
• Thermal wraps
• Intravascular cooling catheters
• Pre-ROSC Intranasal Colling Effectiveness Trial (PRINCE)—nasopharyngeal cooling using a perfluorocarbonaerosol given via a nasopharyngeal cannula
Monitoring Core Temperature

- Esophagus
- Bladder
- Rectum
- Pulmonary Artery

“Intermediate Monitoring Sites”
GAYMAR III

Not selling this product
Who to cool?
Do Circumstances of Arrest Adequately Predict Outcome?

Conclusions. Anoxia time, duration of CPR, and cause of cardiac arrest are related to poor outcome after CPR, but none of these variables can discriminate accurately between patients with poor and those with favorable outcomes.

Recommendations. Prognosis cannot be based on the circumstances of CPR (recommendation level B).
## Complications

### Table 4. Complications during the First Seven Days after Cardiac Arrest.*

<table>
<thead>
<tr>
<th>Complication</th>
<th>Normothermia</th>
<th>Hypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Bleeding of any severity†</strong></td>
<td>26/138 (19)</td>
<td>35/135 (26)</td>
</tr>
<tr>
<td>Need for platelet transfusion</td>
<td>0/138</td>
<td>2/135 (1)</td>
</tr>
<tr>
<td><strong>Pneumonia</strong></td>
<td>40/137 (29)</td>
<td>50/135 (37)</td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
<td>9/138 (7)</td>
<td>17/135 (13)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2/138 (1)</td>
<td>1/135 (1)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>14/138 (10)</td>
<td>13/135 (10)</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>6/138 (4)</td>
<td>6/135 (4)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>5/133 (4)</td>
<td>9/136 (7)</td>
</tr>
<tr>
<td>Seizures</td>
<td>11/133 (8)</td>
<td>10/136 (7)</td>
</tr>
<tr>
<td>Lethal or long-lasting arrhythmia</td>
<td>44/138 (32)</td>
<td>49/135 (36)</td>
</tr>
<tr>
<td>Pressure sores</td>
<td>0/133</td>
<td>0/136</td>
</tr>
</tbody>
</table>

*HACA study group, NEJM, 2002*
# Potential Adverse Effects

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Endocrine/Metabolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypotension</td>
<td>• Dysglycemia due to decreased insulin secretion</td>
</tr>
<tr>
<td>• Bradyarrhythmia</td>
<td>• Pancreatitis</td>
</tr>
<tr>
<td>• VT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal and Electrolyte</th>
<th>Neuro</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypokalemia during cooling</td>
<td>• Seizures (?)</td>
</tr>
<tr>
<td>• Cold induced diuresis inducing:</td>
<td></td>
</tr>
<tr>
<td>– Hypomagnesemia</td>
<td></td>
</tr>
<tr>
<td>– Hypophosphatemia</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Hematologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hospital or ventilator associated pneumonia</td>
<td>• Worsened coagulopathy/bleeding</td>
</tr>
<tr>
<td>• Sepsis</td>
<td></td>
</tr>
</tbody>
</table>
Prevention of Shivering

• Buspirone
• Serotonin 5HT-1A partial agonists
• Meperidine
• Paralytics

Re-warming

- Started after 24 hours at a rate of no greater than 0.5C/1F per hour
- Neuro status usually cannot be adequately assessed until 72 hours after re-warming secondary to sedative meds typically employed.
- If aggressive K replacement was performed during cooling phase, watch for dangerous hyperkalemia during the re-warming phase
SUMMARY

• Screening of patients:
  – Judgement improves with time
  – Rhythm alone should not exclude patients
    • Most have combined rhythms
    • Information on initial rhythm not always available

• Use of bundles helps with rapid implementation and achieving target temp
  – Performance targets helps
SCOTT & WHITE

PHYSICIAN ORDERS

DIAGNOSIS:

DRUG SENSITIVITY:

HYPOTHERMIA AFTER CARDIAC ARREST HOSPITAL ORDERS

Goal temperature of 33°C is to be achieved as soon as possible (less than 4 hours).

Inclusion Criteria

☐ Age 18 years or older.
☐ Women must be over 50 or have a negative pregnancy test (Do not wait to start cooling).
☐ Cardiac arrest with return of a perfusing rhythm after resuscitation (initial rhythm VF or pulseless VT).
☐ Persistent coma as evidenced by no eye opening to pain after resuscitation (no waiting period required).
☐ Blood pressure is at least 90 mm Hg systolic either spontaneously or with fluid and low to moderate doses of vasopressors (refractory cardiogenic shock may be excluded).
☐ Known time of cardiac arrest (excludes “found down” of unknown duration).

Exclusions:

☐ Another reason to be comatose (e.g. drug overdose, status epilepticus).
☐ Pregnancy.
☐ Initial resuscitation lasting more than 1 hour.
☐ Pre-existing DO NOT INTUBATE code status and the patient is not intubated as part of resuscitation efforts.

1. Immediately place ice packs under the armpits, next to the neck, on the torso and the limbs.
2. Temperature sensing Foley catheter should be placed if available, otherwise esophageal, rectal or tympanic...
1. Immediately place ice packs under the armpits, next to the neck, on the torso and the limbs.
2. Temperature sensing Foley catheter should be placed if available, otherwise esophageal, rectal or tympanic temperatures should be used (in that order).
3. Place cooling blankets on top of and under the patient.
   a. Use Arctic 2000 cooling device if available.
4. Do not use ventilator humidifier/heater. A HME may be employed.
5. Administer midazolam 2-6 mg/hour IV and fentanyl 25-75 mcg/hour IV
6. Neuromuscular blockade may be used to control shivering once the patient is adequately sedated.
   a. Neuromuscular blocking agents should be used as outlined in the neuromuscular blockade protocol.
7. Once the patient reaches 33°C (bladder, rectal, or tympanic), keep patient at 33°C by removing ice packs.
8. Begin rewarming 24 hours after the beginning of cooling over a period of 12 hours.
   a. Adjust settings on cooling blanket to increase temperature no more than 1° degree C per every 4 hours until normothermia is achieved (37°C).
9. Neuromuscular blockade should be discontinued once rewarming is initiated.

**Consults**


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**Date**

**Time**

**Physician Last Name (Print)**

**Pager**

**Physician Signature**

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**Rev. 5/07 dill 5/24/07**
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