Brain Protection After Cardiac Arrest

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University of Texas Medical School at Houston
1. Examine the indications for targeted temperature management after cardiac arrest
2. Evaluate the impact of therapeutic hypothermia on prognosis

OBJECTIVES
I have received research funding from Haemonetics Inc. and honoraria from Bard Medical.

DISCLOSURES
# United States 2013

## Out-of-Hospital Cardiac Arrest

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Bystander CPR (overall)</th>
<th>Survivor rate* (overall)</th>
</tr>
</thead>
<tbody>
<tr>
<td>359,400</td>
<td>40.1%</td>
<td>9.5%</td>
</tr>
</tbody>
</table>

## In-Hospital Cardiac Arrest

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Survival rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults</td>
</tr>
<tr>
<td>209,000</td>
<td>23.9%</td>
</tr>
</tbody>
</table>

*survival to hospital discharge
Mechanisms of brain injury

Sudden loss of blood flow

Global hypoxic-ischemic injury

Reperfusion injury
Hypothermia

Destructive processes following ischemia/reperfusion that can be prevented or significantly mitigated by hypothermia.

Black lettering = early mechanisms
Gray lettering = late mechanisms

The three phases of hypothermia treatment

Induction phase: Start of cooling

Beginning of maintenance phase.

Beginning of re-warming phase.

Maintain controlled normothermia after hypothermia phase.

Core temperature (°C)

Cooling rate = 3.0°C/hour
= (36.0°C - 32.0°C/1.33 hr)

Target temp = 32.0°C

Elapsed time (minutes)

80 min

Target temp 0.1–0.5°C

• 275 survivors of witnessed out-of-hospital VT/VF arrest
• Mild therapeutic hypothermia 32-34°C for 24 hours
• Passive rewarming
• Primary endpoint: favorable neurologic outcome (CPC 1-2) at 6 months

<table>
<thead>
<tr>
<th>Cerebral Performance Category</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Good recovery</td>
</tr>
<tr>
<td>2</td>
<td>Moderate disability</td>
</tr>
<tr>
<td>3</td>
<td>Severe disability</td>
</tr>
<tr>
<td>4</td>
<td>Vegetative state</td>
</tr>
<tr>
<td>5</td>
<td>Death</td>
</tr>
</tbody>
</table>
**Table 2. Neurologic Outcome and Mortality at Six Months.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Normothermia</th>
<th>Hypothermia</th>
<th>Risk Ratio (95% CI)*</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable neurologic outcome‡</td>
<td>54/137 (39) 75/136 (55)</td>
<td>1.40 (1.08–1.81)</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>76/138 (55) 56/137 (41)</td>
<td>0.74 (0.58–0.95)</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

*The risk ratio was calculated as the rate of a favorable neurologic outcome or the rate of death in the hypothermia group divided by the rate in the normothermia group. CI denotes confidence interval.

†Two-sided P values are based on Pearson’s chi-square tests.

‡A favorable neurologic outcome was defined as a cerebral-performance category of 1 (good recovery) or 2 (moderate disability). One patient in the normothermia group and one in the hypothermia group were lost to neurologic follow-up.

NNT = 6

p=0.02
• 77 patients resuscitated from VF arrest
• Cooling initiated in field
• Target temperature 33°C
• Active rewarming at 18 hours
• **Primary outcome**: based on disposition
  – Good outcome: discharge to home or rehab facility
  – Poor outcome: death in hospital or discharge to long-term nursing facility

Good outcome

- Hypothermia: 21/43 (49%)
- Normothermia: 9/34 (26%)
- $p=0.046$

No significant differences in mortality
Therapeutic Hypothermia After Cardiac Arrest
An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

Summary: ILCOR Recommendations
On the basis of the published evidence to date, the ILCOR ALS Task Force has made the following recommendations:

• Unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours when the initial rhythm was VF.
• Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest.
950 patients OHCA

Any initial cardiac rhythm

Maintained at target temperature for 36 hours

Rewarmed to 37°C and maintained <37.5°C until 72 hours

33 or 36 degrees?

More liberal goal of 36 with aggressive fever control may have similarly beneficial effect

When to start?

- 1359 patients
- OHCA all causes
- Effectively lowered temperature at time of arrival to ED
- No differences in outcome or survival
- Higher rates of repeat CA in the field, longer time to arrival, increased pulmonary edema

What if not VT/VF?

• Initial rhythm PEA/asystole in 60% OHCA
• Testori et al.
  – 374 non-shockable OHCA (135 hypothermia, 239 non-hypo)
  – Improved neurologic outcome (35% vs. 23%; p=0.024)
  – Decreased mortality (61% vs. 75%; p=0.025)
• Lundbye et al.
  – Location of arrest (in- or out-of-hospital) did not impact outcomes

No suggestion that hypothermia is less safe in PEA/asystole or in-hospital arrest and may improve outcomes

Shivering

Metabolic Impact of Shivering During Therapeutic Temperature Modulation
The Bedside Shivering Assessment Scale

Neeaj Badjatia, MD, MSc; Evangelia Strongilis, RD; Errol Gordon, MD; Mary Prescutti, RN; Luis Fernandez, MD; Andres Fernandez, MD; Manuel Buitrago, MD, PhD; J. Michael Schmidt, PhD; Noeleen D. Ostapkovich, MSc; Stephan A. Mayer, MD, FCCM

Table 1. The Bedside Shivering Assessment Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None: no shivering noted on palpation of the masseter, neck, or chest wall</td>
</tr>
<tr>
<td>1</td>
<td>Mild: shivering localized to the neck and/or thorax only</td>
</tr>
<tr>
<td>2</td>
<td>Moderate: shivering involves gross movement of the upper extremities (in addition to neck and thorax)</td>
</tr>
<tr>
<td>3</td>
<td>Severe: shivering involves gross movements of the trunk and upper and lower extremities</td>
</tr>
</tbody>
</table>

# Shivering Treatment

<table>
<thead>
<tr>
<th>STEP</th>
<th>Intervention</th>
<th>Dose</th>
</tr>
</thead>
</table>
| 0    | Acetaminophen, Buspirone, Magnesium Sulfate, Skin Counterwarming | 650 - 1000 mg every 4-6 hours  
30 mg every 8 hours  
IV replacement for goal serum level (3-4 mg/dL)  
43 C / MAX Temp |
| 1    | Meperdine, Fentanyl, Dexmedetomidine | 50-100mg IM or IV  
Infusion starting dose 25mcg/hr  
Loading 1 mcg/kg, then 0.3-1.5 mcg/hr |
| 2    | Propofol                          | Propofol 50 - 75 mcg/kg/min                    |
| 3    | Vecuronium                        | 0.1-0.15 mg/kg IV every hour                   |
Practice Parameter: Prediction of outcome in comatose survivors after cardiopulmonary resuscitation
(an evidence-based review)

Report of the Quality Standards Subcommittee of the American Academy of Neurology

E.F.M. Wijdicks, MD; A. Hijdra, MD; G.S. Young, MD; C.L. Bassetti, MD; and S. Wiebe, MD

Prognosis

Prognostication after hypothermia

Questions

– How long to wait?
  • 72 hours after rewarming
– Composite of findings?
– Effect of TTM?

De Georgia M, Raad B. Continuum (Minneap Minn). 2012;18(3):515-531
Conclusions

• Comatose survivors of CA should undergo TTM to either 33°C or 36°C
• Initiate TTM at the time of hospital presentation
  – Cooling prior to hospital arrival has not been shown to provide additional benefit
• Fever should be avoided
• Shivering should be treated
• Select patients with non-shockable rhythm or in-hospital arrest should be offered TTM
• Consider delayed prognostication beyond traditional 72 hour time period
• Review guidelines