Neurological Resuscitation after Cardiac Arrest

Managing the patient during Induction, Maintenance, and Rewarming...

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Director of Neurocritical Care

Disclosures

• No financial conflicts
• **ALL** applications described are off-label!
• Grant support from MMC NSI and MRC

http://www.neurocriticalcare.org
http://www.hypothermianetwork.com/INTCAR.htm
Epidemiology of OHCA

- Cardiac arrest is common
  - 295,000 OHCA per year in US
    - 23% VF
    - 31% Bystander CPR
  - Median survival all rhythms 7.9%, VF 21%
    - 17.5% survival to hospital discharge
    - 34% VT/VF subgroup
  - IHCA adults: 19% (despite 95% witnessed or monitored)

- Mortality among patients surviving to be hospitalized
  - Ontario 72% (1994-2002)
  - Taipei 75% (2003-4)
  - Goteborg 68% (2003-5)
  - Rochester 65% (1998-2001)

Circulation 2010;Jan 26:e12-13
Is the cup half empty?

- Nationally, the survival rate of OHCA is < 8%
- Half of patients who survive to be hospitalized die in the hospital
- Half of those who are discharged from the hospital have neurological disability
- Why bother?

...or half full?

- 40% of MMC OHCA survivors have GNO
- 55-60% with VT/VF & without shock have GNO
- A statewide program in Az of bystander CPR, CCR, and hypothermia led to a tripling of OHCA survival!
- These patients have a chance
Northern Hypothermia Network

NHN CA outcomes

- 37 centers, 7 countries
- 986 patients received TH after CA 2004-2008
- 26% CPC 1-2 among asystole/PEA

Factors associated with survival

<table>
<thead>
<tr>
<th>Predictors of outcome</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>5% /year</td>
</tr>
<tr>
<td>Time to ROSC</td>
<td>6% /min</td>
</tr>
<tr>
<td>Initial rhythm VT/VF</td>
<td>2.52</td>
</tr>
<tr>
<td>Witnessed arrest</td>
<td>1.88</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.65</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>0.69</td>
</tr>
<tr>
<td>Initial rhythm asystole</td>
<td>0.56</td>
</tr>
<tr>
<td>Seizures</td>
<td>0.37</td>
</tr>
</tbody>
</table>

From what do “survivors” die…?

Mechanisms of brain injury in circulatory arrest

- **Primary Injury:**
  - “Energy failure” due to ATP depletion
- **Secondary injury:**
  - Loss of transcellular electrolyte gradients
    - $\text{Ca}^+$, $\text{Na}^+$, $\text{Cl}^-$ enter, $\text{K}^+$ exit cell
    - Water follows $\text{Na}^+$ into cells causing cytotoxic edema
  - Lipid peroxidases damage membranes
  - Neurotransmitter release causes excitotoxicity
  - Activation of apoptotic pathways
  - Microvascular thrombosis
  - Reperfusion injury

Laver. Intensive Care Med 2004;30:2126
Other secondary injury…

- Uncontrolled seizure activity
- Hypotension, hypoperfusion
  - Postresuscitation syndrome
  - ICP crisis
  - Autoregulatory failure
- Fever
- Re-arrest
- Hypoxia
- Derangements of glucose metabolism

The hours after ROSC

- **Mediators of cerebral blood flow after CA:**
  - Changes in blood viscosity
  - Sludging of erythrocytes
  - Development of platelet aggregates
    - Heavy concentrations in post-ischemic tissue beds
  - Imbalance of the coagulation system
  - Endothelial flaps
  - Compression by swollen glial cells
  - **Increased cerebral vascular tone and resistance**
Cardiac arrest associated brain injury “CAABI”

- “No flow” affects the most metabolically active areas of brain
  - Cortex
  - Basal ganglia
  - Cerebellum
- “Low flow” affects the watershed areas between vascular territories

75 yo man OHCA 4-2010

- Unwitnessed arrest
- VF on EMS arrival
- 35 minutes CPR and resuscitation
- Therapeutic hypothermia
- 108h after ROSC, GCS 4
- CMO at family request
Pseudolaminar necrosis

Shrunken eosinophilic neuron (anoxic neuron) is the hallmark of HIE

http://www.neuropathologyweb.org/chapter2/chapter2aHIE.html

Rationale for temperature modulation after brain injury

- Hypothermia drives **fatally injured cells** away from lysis and toward apoptosis
- Hypothermia drives **marginally injured cells** away from apoptosis and toward recovery
- Intracellular calcium mediates injury and most apoptotic pathways

Crit Conn 2008;7(4):16
THE USE OF HYPOTHERMIA AFTER CARDIAC ARREST

DONALD W. BENSON, M.D.
G. RAINIE WILLIAMS, JR., M.D.
FRANK C. SPENCER, M.D.
ADOLPH J. YATES, M.D.

Baltimore, Maryland

DATA FROM TWENTY-SEVEN CASES OF CARDIAC ARREST

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Blood group</th>
<th>Operation or approach to heart</th>
<th>Necropsy</th>
<th>Autopsy</th>
<th>Histo-pathology</th>
<th>Neurological status</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>64</td>
<td>F</td>
<td>AB</td>
<td>Percutaneous septostomy, 4 hr.</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Low; no res.</td>
</tr>
<tr>
<td>15</td>
<td>84</td>
<td>F</td>
<td>O</td>
<td>General anesthesia; gastrostomy; heart repair</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>High; found dead 4 hr.</td>
</tr>
<tr>
<td>16</td>
<td>65</td>
<td>M</td>
<td>O</td>
<td>Browneotomy; local anesthesia</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Dead 4 hr.</td>
</tr>
<tr>
<td>17</td>
<td>70</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair; Browneotomy; local anesthesia</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Dead 4 hr.</td>
</tr>
<tr>
<td>18</td>
<td>80</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Dead 5 days</td>
</tr>
<tr>
<td>19</td>
<td>50</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 6 days; did not respond</td>
</tr>
<tr>
<td>20</td>
<td>75</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; local anesthesia</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Dead 3 days</td>
</tr>
<tr>
<td>21</td>
<td>58</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; local anesthesia</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
<tr>
<td>22</td>
<td>1</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
<tr>
<td>23</td>
<td>70</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
<tr>
<td>24</td>
<td>75</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
<tr>
<td>25</td>
<td>50</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
<tr>
<td>26</td>
<td>75</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
<tr>
<td>27</td>
<td>80</td>
<td>M</td>
<td>O</td>
<td>General anesthesia; heart repair</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 5 days</td>
</tr>
</tbody>
</table>

Anesthesia and Analgesia 1959;38 (6): 423
Clinical evidence for TH after CA

- Largest RCT of TH in OHCA survivors
  - 275 patients randomized to TH or routine care
  - Europe 1996-2001
- Absolute 16% increase in chance of a good neurological outcome
- Absolute 14% decrease in 6 month mortality


**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>Favorable neurologic outcome$^\dagger$</td>
<td>84/117 (71%)</td>
<td>78/138 (56%)</td>
<td>1.40 (1.08-1.81)</td>
<td>0.009</td>
</tr>
<tr>
<td>Death</td>
<td>76/138 (56%)</td>
<td>56/137 (41%)</td>
<td>0.74 (0.58-0.95)</td>
<td>0.02</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.
$^\dagger$Two-sided P values are based on Pearson’s chi-square tests.
$^\ddagger$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.

Clinical evidence for TH after CA

- Australian Randomized clinical trial conducted 1996-1999
- Randomized on alternating days to TH or routine care
- TH: good outcome 49%, routine care good outcome: 26% (p=0.046)


Nonrandomized data

Lausanne

- 55 VT/VF OHCA treated with TH 2002-2004
- Compared to historical controls 1999-02
- Similar DT, severity of illness
- CPC 1-2: 56% vs. 26% pre-TH

Table 4. Outcomes at hospital discharge of cardioverter patients with out-of-hospital cardiac arrest treated with therapeutic hypothermia

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>CPC 1</th>
<th>CPC 2</th>
<th>CPC 3</th>
<th>CPC 4</th>
<th>CPC 5</th>
<th>Total Recovery</th>
<th>Moderate Neurologic Disability</th>
<th>Severe Neurologic Disability</th>
<th>Vegetative State</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic hypothermia</td>
<td>94.4±10</td>
<td>94.1±13</td>
<td>2.5±3.2</td>
<td>0.4±0.9</td>
<td>0.4±0.9</td>
<td>94.1±13</td>
<td>2.5±3.2</td>
<td>0.4±0.9</td>
<td>0.4±0.9</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>Standard resuscitation</td>
<td>94.9±11</td>
<td>94.2±12</td>
<td>2.5±3.0</td>
<td>0.4±0.9</td>
<td>0.4±0.9</td>
<td>94.2±12</td>
<td>2.5±3.0</td>
<td>0.4±0.9</td>
<td>0.4±0.9</td>
<td>1.5±0.9</td>
</tr>
</tbody>
</table>

Effect of the implementation of a therapeutic hypothermia protocol on neurological outcome after out-of-hospital VT/VF arrest.

-Crit Care Med 2006;34:1865

Japan

- 400 patients with variable implementation of TH
- Developed model to isolate the interaction between use of TH and outcomes at different time points.
- No benefit of TH in DT < 15 minutes.

Crit Care. 2010 Aug 16;14(4):R155
What are the risks of TH?

<table>
<thead>
<tr>
<th>Complication</th>
<th>Normothermia</th>
<th>Hypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding of any severity†</td>
<td>26/138 (19)</td>
<td>35/135 (26)</td>
</tr>
<tr>
<td>Need for platelet transfusion</td>
<td>9/138 (7)</td>
<td>17/135 (13)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>40/135 (29)</td>
<td>50/135 (37)</td>
</tr>
<tr>
<td>Seizures</td>
<td>0/138 (0)</td>
<td>0/135 (0)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>14/138 (10)</td>
<td>12/135 (9)</td>
</tr>
<tr>
<td>Hemodilution</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>16/136 (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 sore</td>
<td>9/131</td>
<td>6/136</td>
</tr>
</tbody>
</table>

†The sites of bleeding were mucous membranes, the nose, the urinary tract, the gastrointestinal tract, subcutaneous tissue, and skin, as well as intracerebral and intracerebrospinal sites.

HCASG. NEJM 2002;346:549-56

Skeptic’s arguments

- 3300 patients screened in HACA to enroll 275 over 6 years
  - Does not reflect “real world” experience
  - Most commonly managed patients not included
- Many non–TH patients were allowed to develop fever
  - Unfair comparator?
- Single multicenter RCT should not set standard of care
TTM Trial

• European trial of TH (33C) vs TN (36.5C) in CA survivors
• Niklas Neilsen PI
• (INTCAR founder)

• Multinational trial
• Do we need to “prove” the efficacy of TH, again?
• What are the consequences of a poorly designed or inconclusive trial result?

2005 AHA ACLS Guidelines

• “Unconscious adult patients with ROSC after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours when the initial rhythm was VF (Class IIa).”
• “Similar therapy may be beneficial for patients with non-VF arrest out of hospital or for in-hospital arrest (Class IIb).”
Only 10% patients with OHCA will meet RCT criteria for TH

- The decision to initiate TH is usually based on clinical judgement of risk and benefit, not on proof!

**Risks**
- Infections
- Bleeding
- Need for sedation

**Benefits**
- Strongly neuroprotective
- Decreased mortality
- Better neurological outcome


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**TH after Cardiac Arrest**

- **Clinical criteria for therapeutic hypothermia**
  - No more than 8 hours have elapsed since the return of spontaneous circulation.
  - Encephalopathy is present, typically defined as the patient being unable to follow verbal commands.
  - There is no life-threatening infection or bleeding.
  - Aggressive care is warranted and desired by the patient or the patient’s surrogate decision-maker
    - Terminal underlying disease
    - Impending cardiopulmonary collapse
The Devil’s in the details…

How to cool…

Baltimore, 1955
Portland, Maine, 2006
Basics of Therapeutic Hypothermia

There are 3 phases of treatment:

- **Induction**
  - Rapidly bring the temperature to 32-34°C
  - Sedate with propofol or midazolam during TH
  - Paralyze to suppress heat production

- **Maintenance**
  - Maintain the goal temperature at 33°C
  - Standard 12-24 hours (optimal duration is unknown)
  - Suppress shivering

- **De-cooling (rewarming)**
  - Most dangerous period: hypotension, cerebral edema, seizures
  - Goal is to reach normal body temperature over 12-24h
  - Stop all sedation when normal body temperature is achieved

Induction: how to cool

- **Monitor core temperature**
  - Bladder, esophagus, or central venous/pulmonary arterial

- **Cold fluid**
  - 30cc/kg LR or 0.9%NS over 30 minutes
  - 2-2.5°C temperature reduction
  - No adverse cardiovascular results
  - Rare to cause pulmonary edema

- **Ice packs and cooling mats**
  - Effective, but difficult to control rate of temperature change
  - Overcooling is dangerous
Induction: how to cool

• Commercial cooling devices
  – Servo mechanism varies temperature of circulating water or air (prevents overcooling)
  – External (surface cooling) systems
    • Hydrogel heat exchange pads
    • Cold water circulating through plastic “suit”
    • Cold water immersion – awaiting safety data
  – Invasive (catheter based) systems
    • Heat exchange catheter in SVC or IVC
    • Plastic or metallic heat-exchange catheter

Cold IVF

• Polderman 2005
  – 110 patients, 2-3L over 50’
  – 36.9°C to 34.6°C, MAP increased by 15mmHg, no pulmonary edema

• Bernard 2003
  - 22 patients 30cc/kg LR at 4°C over 30 min: 35.5°C to 33.8°C
  Improvements in MAP, renal function, no pulmonary edema

<table>
<thead>
<tr>
<th>Medications, mg/hr</th>
<th>Before Cooling</th>
<th>During Cooling</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine, n = 54</td>
<td>17.4 ± 12.0</td>
<td>16.2 ± 9.2</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Norepinephrine, n = 56</td>
<td>0.42 ± 0.24</td>
<td>0.22 ± 0.18</td>
<td>.01</td>
</tr>
<tr>
<td>Dobutamine, n = 24</td>
<td>34.1 ± 32.2</td>
<td>32.2 ± 41.3</td>
<td>NS</td>
</tr>
<tr>
<td>Esmolol, n = 22</td>
<td>3.2 ± 3.6</td>
<td>3.0 ± 3.0</td>
<td>.13</td>
</tr>
</tbody>
</table>

Bernard. Resuscitation 2003;56:9
Cold IVF

- 2-3L of Ringers or Saline at 4C decreases body temperature
  - No effect on LVEF by echo
  - Improved hemodynamic indices

Kim. Circulation 2005;112:715
Induction – How I do it

- Examine and place BIS monitor
- Give 30-40cc/kg IVF at 4°C over 30 minutes – LR or NS
  - Pressure bag, not IV pump
- Sedate and paralyze the patient
- Apply a commercial cooling device
- Monitor and replace potassium and magnesium
- Antibiotics, usually
- Ventilate to a normal pH, and PaO2>110
- Maintain a MAP > 80
- CVC, Arterial catheter, CO/CI/SVV device

Comparison of cooling methods

- Traditional cooling
  - inexpensive & available
  - Effective
  - Very high incidence overcooling
- Noninvasive cooling devices
  - Safe – no insertion, lots of clinical experience
  - Effective, unless patients very heavy
  - Expensive
- Invasive cooling devices
  - Most effective at tight temperature control
  - Better for heavy patients
  - Insertional dangers: thrombosis, infection, placement-related injury
  - Expensive

Crit Care 2007;11:R91
Clinical paper

Therapeutic hypothermia after cardiac arrest: A retrospective comparison of surface and endovascular cooling techniques

Michael A. Gillies, Rosalie Pratt, Craig Whiteley, Jamie Borg, Richard J. Beale, Shane M. Tibby

1 Department of Intensive Care, Guy’s and St. Thomas’ NHS Foundation Trust, Westminster Bridge Road, London SE1 7EH, United Kingdom
2 Department of Pediatric Intensive Care, Evelina Children’s Hospital, Guy’s and St. Thomas’ NHS Foundation Trust, Westminster Bridge Road, London SE1 7EH, United Kingdom

Table 2

<table>
<thead>
<tr>
<th>Complication</th>
<th>All patients</th>
<th>Endovascular</th>
<th>Surface</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival (median [IQR])</td>
<td>15 (18%)</td>
<td>4 (10%)</td>
<td>11 (27%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Overall survival (mean ± SD)</td>
<td>37.2 ± 12.2</td>
<td>15.8 ± 12.3</td>
<td>19.8 ± 12.8</td>
<td>0.03</td>
</tr>
<tr>
<td>Target not reached</td>
<td>13.1 ± 18.8</td>
<td>3.7 ± 7.8</td>
<td>10 (24%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cooling</td>
<td>42 ± 32</td>
<td>2 (5.1)</td>
<td>3 (7.3)</td>
<td>0.68</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>18 (22%)</td>
<td>10 (26%)</td>
<td>8 (20%)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0 (0%)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hypoventilation</td>
<td>40 (53%)</td>
<td>29 (80%)</td>
<td>1 (25%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Bleeding</td>
<td>7 (9%)</td>
<td>6 (16%)</td>
<td>1 (25%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Fibrillation</td>
<td>5 (6%)</td>
<td>2 (5.1)</td>
<td>3 (7.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>14 (17%)</td>
<td>5 (12%)</td>
<td>9 (22%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Anticoagulation complication</td>
<td>73 (88%)</td>
<td>39 (91%)</td>
<td>35 (85%)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resuscitation (Winter Leonard x^2 = 9.66, p = 0.28, shrinkage = 0.005)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endovascular cooling</td>
<td>0.07</td>
<td>(0.35–2.70)</td>
</tr>
<tr>
<td>APACHE II</td>
<td>1.17</td>
<td>(1.05–1.31)</td>
</tr>
<tr>
<td>Non-VF/VT</td>
<td>1.36</td>
<td>(1.15–5.31)</td>
</tr>
<tr>
<td>Time to ROSC</td>
<td>1.01</td>
<td>(0.98–1.04)</td>
</tr>
<tr>
<td>Hospital mortality (Winter Leonard x^2 = 3.46, p = 0.08, shrinkage = 0.787)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endovascular cooling</td>
<td>1.24</td>
<td>(0.45–3.42)</td>
</tr>
<tr>
<td>APACHE II</td>
<td>1.32</td>
<td>(1.01–1.74)</td>
</tr>
<tr>
<td>Non-VF/VT</td>
<td>1.42</td>
<td>(1.17–1.67)</td>
</tr>
<tr>
<td>Time to ROSC</td>
<td>1.01</td>
<td>(0.98–1.04)</td>
</tr>
<tr>
<td>Poor neurological outcome (Winter Leonard x^2 = 4.98, p = 0.09, shrinkage = 0.001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endovascular cooling</td>
<td>1.65</td>
<td>(0.58–4.74)</td>
</tr>
<tr>
<td>APACHE II</td>
<td>1.00</td>
<td>(0.90–1.23)</td>
</tr>
<tr>
<td>Non-VF/VT</td>
<td>0.83</td>
<td>(0.78–1.32)</td>
</tr>
<tr>
<td>Time to ROSC</td>
<td>1.01</td>
<td>(0.98–1.04)</td>
</tr>
</tbody>
</table>

Abbreviations: VF, ventricular fibrillation; VT, ventricular tachycardia; ROSC, return of spontaneous circulation.

1 Odds ratio per one point increase in APACHE II score.

2 Odds ratio per 1 minute increase in ROSC. In all models global shrinkage was approximately 0.60, illustrating an acceptable signal-to-noise ratio.
Utility of the Medivance Arctic Sun for TH after Cardiac Arrest

- **Effective at Induction**
  - 80% within 4h
  - 90% within 6h
  - 100% within 9h
  - 2 pts got adjuvant cooling:
    - ice or fluids

- **Effective at maintenance**
  - 96.7% of the maintenance phase was spent in the target temperature range

Jarrah. Neurocrit Care 2009;11:S23

90 patients with OHCA – VF arrest and TH randomized
- 72-108mg/dl
- 108-144mg/dl

- Hypoglycemia defined as <54mg/dl

- Moderate hypoglycemia
  - 18% vs 2%

- No mortality difference (33% vs 35%)
Measurement of Blood Glucose

- MMC prospectively enrolled 12 CA survivors and measured concurrent AG, VG, FBG
- Mean glucose values higher during TH
- >20% discrepancy FBG vs AG in 5% when T>36°C, and 17% when T<34°C
- FBG values uniformly higher than AG values

Maintenance: How I do it

- Surface cooling for most patients with bladder or esophageal temperature
- Intravascular cooling if they need a CVC, have skin problems, or if I have extra time
- cEEG
- CO/CI and preload monitoring
- MAP > 80
- Bispectral index when paralyzed to make sure they’re “out”
Five patients who were not out

- 5/204 awoke during TH after CA
- All witnessed arrests
  - 0-1 minute low flow
  - 13-24 minutes No flow
- “BIS1” = BIS after first dose of NMB
- BIS1: 43,52,54,52,63
- All were receiving propofol and/or fentanyl

De-cooling

- Vasodilation causes hypotension
  - May require several liters IVF, increased vasopressors
- More shivering
- Inflammation increases at higher temperature
  - “post-resuscitation” syndrome
- Increased ICP
- Watch for hyperkalemia
  - Primarily in renal failure
- SEIZURES
Patients do not like to rewarm, even if you call it “decooling”.

Shivering

- Drives up systemic metabolic rate
  - Increased CO2 production
  - Increased O2 consumption
  - Major cardiac stressor
- Drives up cerebral oxygen consumption
  - Favors ischemia
- Uncomfortable

BIS monitor can be used to quantify shivering

- EMG dB from BIS monitor correlated with the validated BSAS
- EMG power correlates with rate of cooling

Shiverplots
Shiverplots

- Each additional “shivering episode” associated with 35% increase in odds of GNO

Management of shivering

- Neuromuscular blockade
  - Vecuronium bolus 0.1mg/kg prn BSAS≥2
  - Cisatricurium in renal failure
- Propofol
- Alpha blockade
  - Dexmedetomidine infusion or clonidine
- Scheduled acetaminophen, bupropion
- Meperidine or fentanyl
- Focal counterwarming
- Magnesium infusion (serum level 3-4mg/dl)
Sedation and analgesia during therapeutic hypothermia

- Comfort
- Antiepileptic effects
- HCASG
  - Midazolam 0.125mg/kg/hr
  - Fentanyl 2mcg/kg/hr
  - Pancuronium 0.1 mg/kg q2h

- 70kg man/32h
  - 280mg midazolam
  - 4480mcg fentanyl
  - 224 mg pancuronium

- That’s a lot of drugs!

Drug metabolism during hypothermia: what do we know?

- Propofol concentrations 30% higher at 34°C than 37°C (healthy volunteers)
- Fentanyl concentrations ↑ 5%/↓4°C (healthy swine)

2010 Miracle on Ice Conference
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Seizures prior to therapeutic hypothermia

- 19-34% incidence overall
- Myoclonic status epilepticus traditionally associated with 100% mortality
- NCSE present, less common due to absence of NMB
- Patients rarely received propofol or BDZ

-Neurology 1988; 38:401–405
-Intensive Care Med 2006; 32: 836–842
What do the seizures mean?

- Are they markers for terrible and irreversible brain injury?
- Are they causing active, ongoing injury?
- Should we treat?
- If so, how?
ICU care following CA

- Many techniques for performing TH
- Electrolytes
- Glucose management
- Management of shivering
- Perfusing BP

- Seizure detection
- Antibiotics for aspiration or ALI
- Analgesedation
- Medication dosing

Hospital size and CA outcome

Mortality was lower at urban, teaching, and large hospitals

>109,000 patients in the NIS

CA volume vs outcomes

- 4674 patients from 39 hospitals
- Overall mortality was 56.8%
  - Not all patients comatose
- After adjusting for age and severity of illness, institutional mortality ranged from 46% to 68%
- Annual case volume strongly associated with outcome

Table 1: Results of the logistic regression model for in-hospital mortality for patients admitted to the ICU after cardiac arrest.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 units)</td>
<td>1.16</td>
<td>1.11 - 1.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anaesthetized (yes: no: n: 1000)</td>
<td>1.20</td>
<td>1.19 - 1.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS on ICU admission (per 1 point)</td>
<td>0.94</td>
<td>0.91 - 0.98</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Resuscitation. 2009 Jan;80(1):30-4

Thank You!

Horstmann et al. Brain atrophy in the aftermath of cardiac arrest. NEUROLOGY 2010;74:306-312