Therapeutic Hypothermia
ICU management of the Post-Cardiac Arrest Patient

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Speaker disclosures

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Case: History

• 37 yo 4th year dental student collapses while taking an exam
• She remains untouched for 5 minutes
• Proctor checks for a pulse
• Starts CPR, calls for AED
• AED → shock advised
• Shocked once into perfusing rhythm
Case: 37 yo VF arrest

- Time to ROSC = 8 minutes
- 911 called, patient remains comatose
- Patient arrives to the ED
  - 25 min after arrest, 15 min after ROSC
  - Sinus tachycardia @ 110 beats per minute
  - BP = 132/80
**Case: 37 yo VF arrest**

- Quick neurologic assessment
  - Eyes were closed
  - Not making any verbal sounds
  - Decorticate posturing
  - GCS = 5 (E-1; V-1; M-3)

**Should this woman be cooled?**
Case: 37 yo VF arrest

• Orally intubated
• EKG – NSR with nonspecific ST changes
• 2L of chilled saline infused through peripheral IVs ~1 ¼ hours post-ROSC
• Ice packs placed in groin and axillae
• Arterial line and CVC placed
• Patient is transported to the ICU

What’s next?
Timeline

- ACLS Arrest
- ROCS
- Evaluate For TH
- Induce TH
- Target Temperature Achieved
- Begin Rewarming
- Rewarming Completed
- Maintain Normothermia
- EMS
- ED
- ICU
- Maintenance Phase
- ICU
• Temperature management
• Paralysis and sedation
• Seizures
• Ventilator management
• Fluid and electrolyte shifts
• Infection surveillance/control
• Glucose control
• Resuscitation strategies
Temperature Management

- **Induction**
  - Getting to desired goal (33°C)
- **Maintenance**
  - Keeping the patient at the desired temp for a predefined period of time
- **Rewarming**
  - Returning to normothermia
How are people cooled?

- **Ice packs**: 43% Initiation, 17% Maintenance
- **Cold fluid**: 80% Initiation, 0% Maintenance
- **Air Cooling**: 9% Initiation, 8% Maintenance
- **Water blanket**: 47% Initiation, 63% Maintenance
- **Intravascular**: 10% Initiation, 16% Maintenance

Temperature Deviation

Choose device with a feedback loop

Temperature Monitoring

• PA catheter
• Esophageal
• Bladder
  – If patient has adequate UO
    • 0 – 30 cc/hr – varies per manufacturer
• Rectal/skin/tymppanic less accurate
How long to cool?

- Bernard: 12 hours
- HACA: 24 hours from onset of cooling
- Nielsen: 12 – 48 hours (93% for 24 hours)
- Nagao: Tailored to the patient
  - <15 minutes to ROSC → 24 hours
  - 15-30 minutes to ROSC → 48 hours
  - >30 minutes to ROSC → 72 hours
- Experimental data suggests apoptotic period = 7 days
How fast to rewarm?

- Rapid rewarming associated with increased ICP in stroke/TBI patients
- Bernard: 6 hrs with heated-air blankets
- HACA: Passive rewarming over 8 hrs
- Nielsen: 4 – 12+ hrs (no difference in outcomes)
- Nagao: Rewarmed to 35°C, maintained 24 hrs, then further rewarming

How long to cool?

Suggest cooling for 24 hours.

Active rewarming at max 0.5°C/hr.

Bernard, Hypo

55% Good Outcome

Bernard, Control
Sedation

• Reduces oxygen consumption
• Can prevent shivering
• More rapid cooling
• Used in 2 NEJM trials
• May delay prognostication
• May contribute to hypotension
Sedation

- Short acting
  - Propofol
  - Dexmedetomidine
- Use published sedation scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Overtly combative, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes tube(s) or catheter(s); aggressive</td>
</tr>
<tr>
<td>+2</td>
<td>Agitated</td>
<td>Frequent non-purposeful movement, fights ventilator</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Anxious but movements not aggressive vigorous</td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td>Not fully alert, but has sustained awakening</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(eye-opening/eye contact) to voice (≥10 seconds)</td>
</tr>
<tr>
<td>-1</td>
<td>Drowsy</td>
<td>Briefly awakens with eye contact to voice (&lt;10 seconds)</td>
</tr>
<tr>
<td>-2</td>
<td>Light sedation</td>
<td>Movement or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>-3</td>
<td>Moderate sedation</td>
<td>No response to voice, but movement or eye opening to physical stimulation</td>
</tr>
<tr>
<td>-4</td>
<td>Deep sedation</td>
<td>No response to voice or physical stimulation</td>
</tr>
<tr>
<td>-5</td>
<td>Unarousable</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>
Case: 37 yo VF arrest

- Arrives in the ICU
- T° probe bladder catheter placed
- Surface cooling initiated and target set @ 33°C
- Propofol gtt started
COOLING CURVE

Unable to reach goal

34°C
Paralytics given

32°C
COOLING CURVE

34°C
Icepacks removed

32°C
Paralytics given

Unable to reach goal
COOLING CURVE

Unable to reach goal

Paralytics given

Rewarming Begun

Icepacks removed

34°C

32°C
Paralysis

- Eliminates shivering
  - Decrease MVO$_2$
- No associated hypotension
- Continuous paralysis in 2 NEJM studies
- Must sedate prior to paralyzing
- Seizures may be concealed
- Continuous EEG monitoring recommended
Seizures

• Occur in 5 – 15% who achieve ROSC
  – 10 – 40% of those who remain comatose
• Increase cerebral metabolism 3-fold
• Thiopental and phenytoin are neuroprotective in animal model
• No data on seizure prevention
• Good neuro outcomes reported in patients initially with status epilepticus

Ventilator Management

- Most patients with ROSC don’t have ALI
- Standard ventilator mode/strategy
- Guidelines emphasize 100% FiO₂ during CPR
- Clinicians frequently maintain 100% O₂
- Early hyperoxia harms postischemic neurons
Oximetry-Guided Reoxygenation Improves Neurological Outcome After Experimental Cardiac Arrest

Irina S. Balan, PhD, Gary Fiskum, PhD, Julie Hazelton, MS, Cynthia Cotto-Cumba, MD, and Robert E. Rosenthal, MD

From the Departments of Anesthesiology (I.S.B., G.F., J.H., R.E.R.) and Surgery (C.C.-C., R.E.R.), Program in Trauma, University of Maryland School of Medicine, Baltimore, Md

- 100% FiO₂ v SpO₂ guided oxygenation
- Dog model cardiac arrest with ROSC

Resusc with 100% FiO₂

1 hour of 100% FiO₂

Rapid titration of FiO₂ to SpO₂

Ventilator Management

- Cerebrovascular reactivity to \( \text{PaCO}_2 \) preserved
- No data to support specific \( \text{PaCO}_2 \)
- Hyperventilation may produce cerebral ischemia
- Hypoventilation may increase ICP

Target normocarbia

Fluid and Electrolytes

- Cold diuresis
  - Venoconstriction, ↑ANP, ↓ADH, & tubular dysfunction
- If uncorrected
  - Hypovolemia → hypoperfusion
  - Hemoconcentration → hyperviscosity
- Rewarming, may unmask hypovolemia
- IVF load (w/o K⁺) pre- and during rewarming
Fluid and Electrolytes

- Decreased electrolytes
  - $K^+$, Mg, Phos
- Diuresis induced renal excretion
- Intracellular electrolyte shifts
  - Shift extracellular with rewarming
  - Prevented with slow controlled rewarming
- Replace to low normal during cooling
  - If increased, treat before rewarming
Infection

- Infections are common
- Trends toward more infection with TH
- Suppressed inflammatory response
- Pneumonia caused by aspiration or vent is most-important complication
  - Up to 70% of patients after OHCA
- No data on prophylactic antibiotics

**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>no./total no. (%)</td>
</tr>
<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>0/138</td>
<td>2/135 (1)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>40/137 (29)</td>
<td>50/135 (37)</td>
</tr>
<tr>
<td>Sepsis</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>

*None of the comparisons between the two groups, performed with the use of Pearson’s chi-square test, indicated significant differences.
Infection

• Must be vigilant
  – Signs/symptoms not available
• Inspect lines/tubes, skin, routine CXRs
• Suspect if sudden increase in work of cooling device (↓ water temp)
  – Indicates increase heat production
• Have low threshold to start antibiotics
Glucose Control

• Hyperglycemia
  – Decrease insulin sensitivity
  – Decrease insulin secretion

• Tight glucose control (80-110 mg/dL)
  – Reduced mortality in surgical ICU patients
  – No difference in medical ICU patients
    • If ICU stay $\geq$ 3 days, mortality reduced
    • No difference in subset with neuro disease

• RCT of 90 comatose OH-VF patients
  – Strict (72 – 108 mg/dL)
  – Moderate (108 – 144 mg/dL)
• No difference in 30 day mortality
  – More hypoglycemic episodes in strict

Recommend target value ≤ 144 mg/dL

Oksanen et al. ICM, 2007; 33: 2093-2100.
Resuscitation Strategies

- Post-cardiac arrest syndrome similar to sepsis
- 2005 AHA/ILCOR guidelines recommend hemodynamic optimization of patients post-arrest
  “Providers should try to normalize oxygen content and transport”
• Literature review looking for studies using goal-directed resuscitation post-arrest

• Inclusion criteria
  – Clearly defined intervention consisting of a structured cardiovascular resuscitation protocol
  – Control group in which subjects received standard of care therapy

• NO studies found

Post-Cardiac Arrest Early Goal-Directed Therapy

Who needs this?
- Resuscitated patients with:
  - Pulseless < 60 min
  - Göll Motor score < 6
  - No other reason for coma
  - Not DNR or DNI status
  - If pregnant consult Ob/Gyn

Getting Started
- Stat ECG, echocardiogram, line cardiology consult
- Stat head CT
- Insert arterial pressure monitoring line in radial or femoral artery
- Initiate therapeutic hypothermia if indicated (after arterial line)
- Insert PresPro™ CVC if subclavian or internal jugular vain
- Notify Bed Coordinator for ICU bed and EEG fellow for EEG

MAP
- < 80

CVP
- > 8
- < 80

< 80
- If CVP > 8, give IVF or CHF or significant vasopressor need
- If EF is normal, use NGREPI
- If EF, start DOBUT (2.5-20μg/min)
- If MAP, add DOPA or EPI
- If severe hypotension → IABP

80-100 (Consider lower goal if ACS, CHF, Shock)

ScvO₂ = 65%
- Yes
  - No evidence of shock is present:
    - Optimize CVP if not already done (up to 20)
    - Transfuse PRBC’s if hemoglobin < 10 mg/dl
    - Dobutamine if not already initiated
    - Consider PA Cath if CVP>15 or escalating vasopressors
  - No

ScvO₂ < 65% w/shock?
- No
  - Yes
    - Re-evaluate to achieve goal
    - Consider IABP

MAP, CVP, ScvO₂ goals achieved

Monitor serial lactate to rule out inadequate organ perfusion

ACS=Acute coronary syndrome

Updated 5/16/06
Is it working?

“We can implement early goal-directed hemodynamic optimization while inducing TH w/o negatively impacting time to target T°”

- Analyzed first 18 patients since start of TH
- 18 historic controls from 2001-2005
- Examined differences in
  - Vasoactive drug use
  - Volume resuscitation
  - Mortality
  - Good neurologic outcomes

<table>
<thead>
<tr>
<th>Resuscitation End-Point (hr)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVP ≥ 8 ≤ 20 mmHg</td>
<td>77.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81.3</td>
</tr>
<tr>
<td>MAP 80-100 mmHg</td>
<td>50.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>83.3</td>
</tr>
<tr>
<td>ScvO2 &gt; 65</td>
<td>83.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>93.8</td>
</tr>
<tr>
<td>Target Temp 32-34°C</td>
<td>5.6</td>
<td>11.1</td>
<td>44.4</td>
<td>55.6</td>
<td>61.1</td>
<td>66.7</td>
<td>77.8</td>
</tr>
</tbody>
</table>

Percentage of Patients Reaching End-Point at Specific Time

- Intravenous Fluid Boluses
- Vasoactive Medications
- Inotropic Agents and Blood
- 4°C Chilled Saline; Cooling Wraps

## Vasoactive Agents

<table>
<thead>
<tr>
<th></th>
<th>Hour</th>
<th>EGDHO</th>
<th>Historic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vasopressor</strong></td>
<td>1</td>
<td>38.8</td>
<td>22.2</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>38.8</td>
<td>50.0</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>29.4</td>
<td>28.5</td>
</tr>
<tr>
<td><strong>Inotrope</strong></td>
<td>1</td>
<td>29.4</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>38.8</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>33.3</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Vasodilator</strong></td>
<td>1</td>
<td>27.7</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>33.3</td>
<td>25.0</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>17.6</td>
<td>14.2</td>
</tr>
</tbody>
</table>
## Fluid Balance

<table>
<thead>
<tr>
<th></th>
<th>EGDHO</th>
<th>Historic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ED</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Input</td>
<td>2543.3</td>
<td>812.5</td>
</tr>
<tr>
<td>Output</td>
<td>117.6</td>
<td>125.0</td>
</tr>
<tr>
<td>Balance</td>
<td>2425.7</td>
<td>687.5</td>
</tr>
<tr>
<td><strong>12 Hours</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Input</td>
<td>5761.0</td>
<td>1450.5</td>
</tr>
<tr>
<td>Output</td>
<td>2006.6</td>
<td>1726.5</td>
</tr>
<tr>
<td>Balance</td>
<td>3754.4</td>
<td>-276.0</td>
</tr>
<tr>
<td><strong>24 Hours</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Input</td>
<td>8624.1</td>
<td>4203.0</td>
</tr>
<tr>
<td>Output</td>
<td>3057.7</td>
<td>2851.1</td>
</tr>
<tr>
<td>Balance</td>
<td>5566.4</td>
<td>1351.9</td>
</tr>
</tbody>
</table>
Outcomes Data—76 patients

Survival to discharge

- Normothermia: 22%
- Hypothermia: 51%

87% Neurologically intact
Resuscitation Strategies

• Reasonable goals for PCAR include
  – MAP of 65 to 100 mm Hg
    • Consider patient’s normal BP
    • Cause of arrest
    • Severity of any myocardial dysfunction
  – CVP of 8 to 12 mm Hg
  – \( \text{ScvO}_2 \) 70%
  – Urine Output 1 mL/kg/hr
  – Normal or decreasing serum lactate level
Case: Conclusion

- HD#2 – extubated
- HD #3 – sitting up asking for diet soda
- Normal cath and EP studies
- Cause of arrest
  - Tako tsubo
- AICD placed
- Discharged HD # 11
- Practicing dentist in the Mid-Atlantic
Conclusions

- Hypothermia is a 3 phase process
- Consider routine paralysis for induction
- Treat cold diuresis with IVF
- Check electrolytes frequently and correct aggressively in induction and maintenance
- Monitor for infection, particularly pneumonia
- Consider empiric antibiotics
- Target glucose $\leq 144$ mg/dL
Thank you!

Dave Gaieski
Ben Abella
Bob Neumar
Lance Becker
Roger Band
Sanjay Desai
Howard Cooper
Greg Marchand
Allen Wolfe
Kori Hudson
Brendan Furlong

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