ICE: Induced Cooling by EMS

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Disclosure

Financial relationships include
• Alsisus Corp. - Speaker
• No Honorarium

Hey, Kits! Thinking is for Extras!

Wanna drink the Kool-Aid?
Bring Out Your Dead

The Plan

- Why cool?
- When to cool?
- Who to cool?
- How to cool?
- Cool cases!
The Plan
- Review the data and guidelines surrounding hypothermia after cardiac arrest
- Does time matter?
- Our community’s experience
- “From dispatch to discharge”

Why Hypothermia?
- Of those who survive to hospital admission but do not survive to discharge:
  - 10% die due to recurrent dysrhythmias
  - 30% die due to cardiovascular collapse
  - 40% die to neurologic impairment
  - 20% die due to other causes (sepsis, etc.)
Witnessed Return of Spontaneous Circulation
("heartbeat")
Old CPR v. New CPR Protocols

Presenting Heart Rhythm

All Worked Arrests

All  Asystole  PEA  VFVT
Rhythm Type

% with ROSC

Why Induced Hypothermia?

Pre-hospital ROSC¹
- 45% (38%) of v-fib arrests
- 37% (22%) of all cardiac arrests
Discharge²
- 12% (10%)
Post Resuscitation Deaths³
- 10% die due to recurrent dysrhythmias
- 30% die due to cardiovascular collapse
- 40% die due to PRE
Post Resuscitation Encephalopathy

- Initial insult from cardiac arrest
- Period of luxuriant hyperperfusion
- Cell injury
  - Oxygen free radical formation
  - Inflammatory cascade
  - Glutamate mediated cell death
- Loss of autoregulation
- Sludging and hypoperfusion
- Perfusion/demand mismatch

Optimizing Neurologic Resuscitation

- Mild Induced Hypothermia (IH)
  - Decrease metabolic demand
  - Inhibits inflammatory cascade
  - IH is time sensitive
- Hemodilution
  - Normal saline dilution as part of hypertensive reperfusion strategy
- Hypertensive reperfusion
  - Use of vasopressors to target MAP of 90

Figure 2: Cumulative Survival in the Normothermia and Hypothermia Groups. Censored data are indicated by tick marks.
Metaanalysis

- Short term benefit ratio
  - 1.68; 95% CI 1.29-2.07
- 6 mos benefit ratio
  - 1.44; 95% CI 1.11-1.76
- NNT 6 CI (4-13)

Other NNT
- ASA (MI) 25
- Beta blocker 42
- Cath facility 15
**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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**Circulation**

Post Resuscitation Recommendations
- Induced hypothermia
- Prevention of hyperthermia
- Tight glucose control
- Prevent hypocapnia
- Maintain elevated MAP

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**Side Effects of IH**

- Holzer & Bernard
  - No difference in complication rates in normothermic and hypothermic cohorts
- Potassium shifts
  - Intracellular shift with induction
  - Extracellular shift with warming
- Fluid status
  - Cooling causes diuresis
  - Warming causes hypovolemia
- Respiratory Alkalosis
  - Temperature corrected ABG allows changes in minute ventilation to support normal PaCO2
- Hyperglycemia
  - HACA grp and Bernard found that high blood glucose after cardiac arrest is associated with poor neurologic outcomes but did not find any improvement with tight glucose controls.
Complications of IH in Other Applications

- Neutropenia
  - Neutropenia and increased incidence of pneumonia seen in patients exposed to prolonged hypothermia (>24hrs) in other applications

- Coagulopathy
  - May alter clotting cascade, platelet function

- Cardiac dysrhythmias
  - Little risk for clinically significant dysrhythmias if temperatures are maintained >30°C

Hypothermia

- All guidelines flow from essentially two studies:
  - Bernard
  - HACA
- These studies were published in 2002
- Many remain unconvinced of the data
  - Small numbers of patients
  - Potential confounders

HACA Study Group
**HACA Study Group**

Table 2. Neurologic Outcome and Mortality at Six Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hypothemia</th>
<th>Hypotension</th>
<th>Risk Ratio (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n)</td>
<td>129/137</td>
<td>136/156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reversible neurologic deficit (n)</td>
<td>55/117 (39)</td>
<td>76/136 (55)</td>
<td>1.01 (0.86-1.18)</td>
<td>0.809</td>
</tr>
<tr>
<td>Death (n)</td>
<td>76/136 (55)</td>
<td>54/127 (41)</td>
<td>0.74 (0.58-0.95)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Bernard Study Group**

Table 5. Outcome of Patients at Discharge from the Hospital

<table>
<thead>
<tr>
<th>Outcome*</th>
<th>Hypothemia (N=43)</th>
<th>Hypotension (N=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or minimal disability (able to care for self, discharged directly to home)</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Moderate disability (discharged to a rehabilitation facility)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Severe disability, aware but completely dependent (discharged to a long-term nursing facility)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Severe disability, unconscious (discharged to a long-term nursing facility)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>22</td>
<td>23</td>
</tr>
</tbody>
</table>
“Although we await further studies
With great interest,
We recommend the use of mild
Induced hypothermia
In survivors of cardiac arrest –
As early as possible and for
At least 12 hours”

-- Peter Safar and Patrick Kochanek, NEJM 2002;346(8):612-3

Editorial Comments

“"The reason hypothermia has not become the
standard of care for post-resuscitation is simple. Emergency
and EMS physicians have failed to make
it so."”

Mennegazzi and Callaway, PEC 2005

Editorial Comments

“"This therapy should now be considered
standard of care for these patients””

Bernard S, Critical Care Med 2006
Lack of Money Is the Root Of all Evil

-- George Bernard Shaw

Hypothermia is Free

Cost for our EMS System:

+ $5000 total start up cost
+ ~$4 per patient

Cost in-hospital:

+ ~$100,000 start up costs
+ ~$1,000 per patient

Institutional budget dust

Questions Now

When should we start?

+ During CPR
+ Immediately after ROSC
+ In the Emergency Department
+ In the ICU

Who should receive the treatment?

+ PEA/Asystole
+ Trauma, stroke, head injury, MI
When to cool?

Delay in cooling negates the beneficial effect of mild resuscitative cerebral hypothermia after cardiac arrest in dogs: a prospective randomized study.


<table>
<thead>
<tr>
<th>Group</th>
<th>Deficit Score</th>
<th>Histologic Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normo</td>
<td>44</td>
<td>150</td>
</tr>
<tr>
<td>Immed</td>
<td>19</td>
<td>81</td>
</tr>
<tr>
<td>Delay</td>
<td>38</td>
<td>107</td>
</tr>
</tbody>
</table>

During CPR – Does It Matter?

- A single animal study and Dr. Safar’s editorial suggest it matters
- Animal study demonstrated dramatic increase in neurologically intact survivors when hypothermia was induced at the initiation of resuscitation

-Nozari A et al. Circulation 2006;113:2690-96

During CPR?

- This is possible, with the following concerns:
  - Adequate temperature monitoring
  - Effectiveness of defibrillation
  - Effectiveness of ACLS medications (if these actually matter)
  - Increased cost (minimal, but real)
During CPR – Does It Matter?

<table>
<thead>
<tr>
<th>Resuscitation Variables</th>
<th>Group</th>
<th>CH</th>
<th>EH</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counterstrokes, total</td>
<td>13 (1–50)</td>
<td>1 (1–48)</td>
<td>0.125</td>
<td></td>
</tr>
<tr>
<td>Counterstrokes, total energy, J</td>
<td>275 (150–1471)</td>
<td>195 (150–1516)</td>
<td>0.125</td>
<td></td>
</tr>
<tr>
<td>ROSC, min of CPR</td>
<td>51 (5–235)</td>
<td>16.5 (15–46)</td>
<td>0.395</td>
<td></td>
</tr>
<tr>
<td>Total lactate, mEq</td>
<td>117 (55–175)</td>
<td>95 (40–230)</td>
<td>0.600</td>
<td></td>
</tr>
<tr>
<td>Total epinephrine, mg</td>
<td>2.45 (1.3–4.3)</td>
<td>0.75 (0.3–3)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Total NE, mg</td>
<td>13.86 (5.23–26.64)</td>
<td>17.08 (12.47–172.04)</td>
<td>0.674</td>
<td></td>
</tr>
<tr>
<td>Duration of NE infusion, h</td>
<td>5.3 (3.8–15.6)</td>
<td>30.5 (8.0–45.4)</td>
<td>0.090</td>
<td></td>
</tr>
<tr>
<td>Survival, h</td>
<td>21 (4–46)</td>
<td>46 (48–96)</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

NE indicates norepinephrine. Data are given as median (range).

During CPR – Does It Matter?

<table>
<thead>
<tr>
<th>Delayed hypothermia</th>
<th>Early hypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPC 5 or death</td>
<td>00000000</td>
</tr>
<tr>
<td>OPC 4</td>
<td>0</td>
</tr>
<tr>
<td>OPC 3</td>
<td>0</td>
</tr>
<tr>
<td>OPC 2</td>
<td>0</td>
</tr>
<tr>
<td>OPC 1</td>
<td>0</td>
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</tbody>
</table>

OPC: Outcomes Performance Criteria
During CPR – Will Defib Work?

+ Animal model evaluating shock success at normothermia, moderate hypothermia (33 degrees), and severe hypothermia (30 degrees)

+ Logistic regression demonstrated risk of post-defibrillation asystole to be 18% in the normothermic group vs. 1% in the hypothermic group

During CPR – Will Drugs Work?

+ Animal study for severe hypothermia

+ Purpose was to study treatment for accidental, severe hypothermia with ventricular fibrillation arrest

+ Bottom line: The drugs worked

Wira C et al.  Resuscitation 2006;69:509-16
During CPR – Will Drugs Work?

Summary of “When”

- Evidence suggests earlier is better
- Preliminary animal data suggests we should consider induction during the resuscitation
- Certainly, induction immediately after ROSC appears indicated:
  - Absolutely for VF/VT
  - Probably for other rhythms as well

-109 out of hospital cardiac arrest from all rhythms
- Retrospective study using historical controls
- 55 induced hypothermia and 54 controls
- Cool to 33deg C with external device for 24 hrs
- Patients treated with versed, fentanyl and vecuronium
- MAP were maintained 90-100mmHg
Our Program: ICE
Induced Cooling by EMS
Pearls:

- Criteria for Induced Hypothermia:
  - ROSC after cardiac arrest not related to trauma or hemorrhage
  - Age greater than 16
  - Female without obviously gravid uterus
  - Initial temperature > 34°C
  - Patient is intubated and remains comatose (no purposeful response to pain)
  - If patient meets either criteria for induced hypothermia and is not intubated, then in-hospital according to protocol before inducing cooling. If unable to intubate DO NOT initiate induced hypothermia.
  - When exposing patient for purpose of cooling underguments may remain in place. Be mindful of your environment and take steps to preserve the patient's modesty.
  - Do not delay transport for the purpose of cooling.
  - Reassess airway frequently and with every patient move.
  - Patients develop metabolic alkalosis with cooling. Do not hyperoxygenate.
  - If there is loss of ROSC after cooling is initiated or any other complication as a result of the protocol please complete...
Getting Started

- Process mapping
- Stake holder buy-in
- Establish expectations
- Turn the process over

Process Mapping

- Interoperability of phases of care
  - Dispatch to discharge
- Limited participating hospitals
  - High volume PCI facilities
- Redundancy
  - Same process at any entry point
Induced Hypothermia and/or Rewarming Status Post Cardiac Arrest Orders

**Inclusion Criteria**
- Non Traumatic Cardiac Arrest with return of Spontaneous Circulation (ROSC)
- Core Temperature greater than 93.5°F (34°C) at presentation
- Time in induction of hypothermia is less than 15 minutes
- Duration after ROSC GS for less than 4 hours to purposeful movement to pair

**Exclusion Criteria**
- Uncontrolled G1 bleeding
- Patient requiring intracerebral therapy
- Advanced Directive or DNR status
- Absolute contraindication as evidenced by uncontrollable dysrhythmia
- Refractory hypoxemia (oxygen saturations <90% with pressors – at least 7mmHg)
- Inability to maintain an oral airway
- Severe intracranial hemorrhage
- Major trauma, intraabdominal or intracranial surgery within 14 days
- Cardiac arrest

**DATE/TIME** | **Weight** | **Time of ROSC**
--- | --- | ---

**TIME COOLING STARTED:**

1. Place patient on ice packs on neck, anterior chest, and in groin.
2. Cover patient with ice packs and body bags.
3. Monitor core temperature and rewarming.
4. Monitor for signs of hypothermia or hyperthermia.
5. Monitor for signs of cardiac arrest or other medical complications.
7. Monitor for signs of respiratory failure.
8. Monitor for signs of infection.
10. Monitor for signs of hepatic failure.
11. Monitor for signs of bleeding.
12. Monitor for signs of gastrointestinal bleeding.
15. Monitor for signs of hypoglycemia.
17. Monitor for signs of hypokalemia.
18. Monitor for signs of hypomagnesemia.
19. Monitor for signs of hyperkalemia.
20. Monitor for signs of hypernatremia.
22. Monitor for signs of hypercalcemia.
23. Monitor for signs of hypothermia.
24. Monitor for signs of hyperthermia.
25. Monitor for signs of hypoxemia.
26. Monitor for signs of hyperoxemia.
27. Monitor for signs of acidemia.
28. Monitor for signs of alkalosis.
29. Monitor for signs of metabolic acidosis.
30. Monitor for signs of respiratory acidosis.
31. Monitor for signs of respiratory alkalosis.
32. Monitor for signs of metabolic alkalosis.
33. Monitor for signs of hyperchloremia.
34. Monitor for signs of hypochloremia.
35. Monitor for signs of hypernatremia.
36. Monitor for signs of hyponatremia.
37. Monitor for signs of hyperglycemia.
38. Monitor for signs of hypoglycemia.
40. Monitor for signs of hypokalemia.
41. Monitor for signs of hypermagnesemia.
42. Monitor for signs of hypomagnesemia.
43. Monitor for signs of hypercalcemia.
44. Monitor for signs of hypocalcemia.
45. Monitor for signs of hyperphosphatemia.
46. Monitor for signs of hypophosphatemia.
47. Monitor for signs of hyperuremia.
48. Monitor for signs of hypouricemia.
49. Monitor for signs of hypercholesterolemia.
50. Monitor for signs of hypcholesterolemia.
51. Monitor for signs of hypertriglyceridemia.
52. Monitor for signs of hypotriglyceridemia.
53. Monitor for signs of hyperlipidemia.
54. Monitor for signs of hypolipidemia.
55. Monitor for signs of hypercoagulability.
56. Monitor for signs of hypocoagulability.
57. Monitor for signs of hyperfibrinogenemia.
58. Monitor for signs of hypofibrinogenemia.
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98. Monitor for signs of hypofibrinogenemia.
99. Monitor for signs of hyperfibrinolysis.
100. Monitor for signs of hypofibrinolysis.

**Patient Identification:**

**Date:**

**Time:**
**Stakeholder buy-in**
- Identify all stakeholders
- Present rationale
- Identify key players

**Stakeholders**
- ED
  - Nursing
  - Physicians
- Cardiology
  - Cath lab nursing
  - CCU nursing
  - Cardiologists
- ICU
  - Nursing
  - Intensivists
- Neurology
- Pharmacy
- Hospital Admin

**Expectations**
- Provide sample protocols
- Work product goals
- Deadlines
- Inevitable completion
**Turn the process over**

+ Key to buy in
+ Sense of ownership
+ Daily advocates

**Elements of Prehospital Hypothermia**

+ ROSC
  + Uninterrupted compressions, timely defibrillation, controlled ventilations, efficient dispatch
+ Method of cooling
  + $$ vs. ease of use
+ Hospital coordination
  + Selective destination
  + Continuation of cooling

**Hospital Destination**

+ High volume cardiac catheterization center
+ Post-arrest care may include PCI and transfer while in the 24 hour window is cumbersome
What Have We Done So Far?
- February 2006 – EMS physicians and command staff leadership reviewed literature
- March 2006-August 2006 – Developed community-wide plan for post-resuscitation care
- August 2006-October 4, 2006 – Education regarding the plan
- Implemented plan – October 5, 2006

Old Habits
- One facility wanted to use the HACA criteria strictly
- Was resuscitation started between 5 and 15 minutes after collapse?
- Did the entire code last > 60 minutes?
- Many hesitate to initiate therapy when:
  - Initial rhythm was not VF/VT
  - Patient is going to the cardiac cath lab

Problems – Old Habits
- Reluctance when not v-fib or when going to the cath lab.
- Disparate experience with IH.
- Induction decision based on down time, duration of CPR and neuro exam.
Old Habits

- The immediate post-resuscitation neurologic exam
- One of the reasons we use paralysis – to get people not to do this!
- The immediate post-resuscitation neurologic exam is useless as a prognostic tool

Data from Neurological Literature

A more recent meta-analysis of predictive studies suggested only 4 variables had a high specificity: absent pupillary light reactions on day 3, absent motor response to pain on day 3, bilaterally absent median SSEPs within week 1, and burst suppression or isoelectric EEGs within week 1.


Data From the Neurological Literature

- 2006 Evidence-Based Review of the literature
- A must-read for clinicians caring for victims of cardiac arrest
- None of us are proposing that we fill ICUs with hopeless cases
- It is imperative, however, that we define hopeless in an evidence-based way
- Wijdicks EFM et al. Neurology 2006;67:203–10
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).

Is Elevated Body Temperature Predictive of Poor Outcome?

Conclusions. Elevated body temperature (>37 °C) is associated with poor outcome. However, hyperthermia alone could not discriminate accurately between patients with poor and those with favorable outcomes.

Recommendations. Prognosis cannot be based on elevated body temperature alone (recommendation level C).

Are Physical Exam Findings Predictive of Outcome?

Conclusions. The following clinical findings accurately predict poor outcome (FPR of 0 with narrow CIs); myoclonus status epilepticus within the first 24 hours in patients with primary circulatory arrest, absence of pupillary responses within days 1 to 3 after CPR, absent corneal reflexes within days 1 to 3 after CPR, and absent or extensor motor responses after 3 days.
Are Physical Exam Findings Predictive of Outcome?

Recommendations. The prognosis is invariably poor in comatose patients with absent pupillary or corneal reflexes, or absent or extensor motor responses 3 days after cardiac arrest (recommendation level A). Patients with myoclonus status epilepticus within the first day after a primary circulatory arrest have a poor prognosis (recommendation level B).

Summary of Predictors

+ Situation of CPR and circumstances of resuscitation are not sufficiently predictive of outcome
+ The initial post-resuscitation exam is not predictive of outcome.
Where Does This Leave Us?

- Post-resuscitation patients should receive hypothermia if initial rhythm was VF/VT
- Strong consideration should be given to providing the therapy to other post-resus patients
- Coordination between EMS, EM, ICU, and Cardiology is essential

Where Does This Leave Us?

- Post-resuscitation/cardiac specialty hospitals with expertise in these therapies should receive patients directly from the field or in prompt transfer
- We may be starting all codes cold in the near future

What Have We Found?

- Since October 2006, we have induced over 100 patients
- We have experienced no complications and 2 mild protocol violations
- “Doc, resuscitation is hard – this is easy”
So where are the numbers?

- We have completed survival analysis
- Currently looking at neuro outcomes
- We have submitted abstracts for SAEM in May 2008

Pittsburgh Data at NAEMSP

- OHCA – Results to date
  - 31 OHCA patients
  - 26/27 eligible cooled
  - Survival 47%
  - Good neuro outcome 38%

Thanks to Jon Rittenberger and Frank Guyette

Case #1: Mile High Club

- Male on-board commercial flight
- Developed chest pain
- Was provided ASA and SL NTG from the on-board medical kit
Case #1: Mile High Club

- Shortly after the medication:
  - Patient become unresponsive
  - Suffered cardiac arrest with non-shockable rhythm – CPR
  - Plane was diverted to Raleigh-Durham International
  - Patient was found with weak carotid pulse and no spontaneous respirations

- Patient bit the blade of the laryngoscope
- Modified prehospital protocol with ice packs only
- Intubated in the ED via RSI
- Cath lab with 100% LAD
- 24 hours of IH
- Discharged neurologically intact

Case #2

- 63 year old male
- Witnessed arrest in his home
- Wife performed compression-only CPR via EMD
- Fire and EMS arrived simultaneously
Patient #2
+ Patient was induced on-scene after noting no purposeful response to pain
+ Patient was without sustained ROSC with EMS for 15 minutes
+ Temp on arrival was ~35
+ Patient completed 24 hours of treatment – no neuro response

Patient #2
+ Patient extubated ~48 hours into hospital course
+ Very confused and minimally responsive
+ Some combativeness

Patient #2
+ On hospital day #5, patient with elevated troponins and had non-ST elevation MI
+ Went to cath lab for successful PCI
+ On hospital day #6, patient with return of neuro function save for recent memory
+ D/C home neuro intact
**Patient # 3 (6/2007)**

- 20s year old male
- Warm water drowning with potential substance abuse
- Asystolic with EMS for over 15 minutes (~25 minutes without pulse in total)
- After ROSC, patient received ICE while on-scene

**At the Emergency Dept**

- The reasons why we shouldn’t:
  - “He might have a head injury with ICH”
  - “He might have a spinal cord injury”
  - “He is a trauma patient and we're not sure trauma will do this”
- Patient’s hypothermia therapy was put "on hold" until CT scan results could be obtained

**In the ICU**

- Patient was admitted to trauma services
- Eric Reyer, RN went to the ICU and asked trauma about hypothermia
- Permission was granted to consult the medical intensivist to resume hypothermia
And then . . .

- 36 hours later, patient completed rewarming
- And he did not wake up – at all
- Family was consulted and horrible prognosis was predicted

The Rest of the Story

- On hospital day #11, the patient without warning called his mother by name
- Over the next 24 hours, he regained all cognitive function except for a persistent pause in his speech
- He remains with physical weakness and is undergoing outpatient OT/PT

Summary

- ICE is easy
- It appears to improve outcomes for us
- There are essentially no negatives
- www.wakeems.com/ICE2008
Patient #3

- No drugs, no intubation during resuscitation
- Intubated after ROSC (no RSI)
- No movement to painful stimuli
- Induced on-scene
- Clean cath – held at 33 degrees for 24+ hours
- Complete neurological recovery