Cold and Not-So-Dead: Real life application of therapeutic hypothermia

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Objectives

• Recognize patients eligible for hypothermia

• Understand implementation of a complete care package

• Recognize and treat the sequelae of these treatments

Why Cardiac Arrest?

• Mortality is 95%

• Critically ill patients with bad timing
  - Death does not care about holidays
  - No longer Q04L

• Resource and Emotionally intensive
Can't be Fixed

- Viral infections
- Back Pain
- Abdominal Pain, chronic
- Diabetes
- Fibromyalgia
- RSD
- Headaches
- Dementia
- HTN
- Scleroderma
- Dental Pain
- Sjogren's
- SLE
- Stupidity

Can be Fixed

- Bacterial Infections (Many)
- **Sudden Cardiac Death**

Case Review: DK

- 71 y/o male with witnessed V-fib arrest during a stress test
- Fell striking his head
- Defibrillator at MD office was not functioning
- CPR started immediately
Case Review: DK

- EMS arrived and shocked 3 times into asystole
- Meds given: 6 Epinephrine, 3 Atropine, and Amiodarone
- Total down-time: 25 minutes
- Initial GCS: 3

Out of Hospital Cardiac Arrest - A Common Disease

- 600-1000 Americans will suffer OOHCA today
- 600-1000 Americans will suffer OOHCA tomorrow
- 25+ will suffer OOHCA during this talk
- High morbidity and mortality - 47% never make it to the hospital

Survival after Cardiac Arrest in Pittsburgh

Wang, 2005
Two Hurdles to Consider…

- Cardiac Death- The HARD Way
- Brain Death- The Soft(er) Way
- Must work on both if the patient is to survive

Multiple Ways to Die

Data from Laver (2004)

Therapeutic Hypothermia
Inclusion Criteria

**HACA**
- In ED after ROSC
- Witnessed
- VF / VT
- Presumed Cardiac
- 18-75 years old
- <60 min since collapse
- 5-15 min collapse to resuscitation

**Bernard**
- Arrival at participating ED
- VF / VT
- ROSC
- Coma after ROSC

Exclusions

**HACA**
- Responds to verbal commands
- MAP<60 mmHg x 30 min
- SaO2<85% x 15 min
- Coagulopathy
  - Tympanic temp < 30°C
  - Arrested after EMS arrival
  - Pregnancy
  - Coma before cardiac arrest
  - Terminal illness, in another study, unavailable for follow-up

**Bernard**
- Systolic BP < 90 despite pressors (epinephrine)
  - <18 yrs old for men
  - <50 years old for women (surrogate for pregnancy)
- Alternative cause of coma (Drug OD, head trauma, CVA)
- No ICU bed available

Treatment

**HACA**
- Normothermia (N=138)
  - Standard hospital bed and kept warm
- Hypothermia (N=137)
  - 32-34°C (tympanic and bladder) for 24 hours
  - TherAcool mattress/blanket
  - If not at goal within 4 hours, add ice packs

**Bernard**
- Normothermia (N= 34)
  - Usual care with passive rewarming to 37°C
- Hypothermia (N=43)
  - In field, expose, cold packs to head/torso
  - In ED / ICU, further ice-packs
  - Core temperature of 33°C for 12 hours.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>NNT (mortality)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Goal-directed therapy</td>
<td>7</td>
</tr>
<tr>
<td>Low-dose steroid</td>
<td>10</td>
</tr>
<tr>
<td>ARDSnet low TV ventilation</td>
<td>12</td>
</tr>
<tr>
<td>Activated protein C</td>
<td>17</td>
</tr>
<tr>
<td>Intensive glycemic control</td>
<td>28</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>6.1-7.0</td>
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Optimizing Therapeutic Hypothermia

- **Good Outcome (95% CI)**
  - Favorable Outcome: 1.40 (1.08 - 1.81)
  - Death at 6 months: 0.74 (0.56 - 0.95)

- **Predictive Value**
  - NNT (Favorable Outcome) = 6.4
  - NNT (Not Dead) = 7.0

Relative Risk Reduction:
- Neuro: 26%
- Death: 26%

- **Odds Ratio**
  - Good Outcome: 2.65 (1.02 – 6.88)
  - Good Outcome: 5.28 (1.47 – 18.76)

- **Other**
  - NNT (Good Outcome) = 4.5
  - NNT (Not Dead) = 6.1
  - Relative Risk Reduction (Neuro) = 30%
  - Relative Risk Reduction (Death) = 24%
Let’s Do It!

Umm...
How?

Who?
**Who do we cool?**

- The Mostly Dead

**2005 AHA Consensus Statement**

Class IIA
- Comatose adult pt with ROSC after out of hospital V-Fib cardiac arrest
  - Should be cooled to 32-34°C for 12 - 24 hrs

Class IIB
- Comatose adult pt with ROSC with non V-Fib cardiac arrest both in/out hospital arrest
  - Should be cooled to 32-34°C for 12 - 24 hrs

**Simplified entry criteria**

- Suffered cardiac arrest
  - Chest compressions or rescue shock
- Comatose after cardiac arrest
  - Not following verbal commands
Effects of Hypothermia

- First, it prevents HYPERTHERMIA
  - For each 1°C over 37°C for $T_{max}$ during the first 48 hours, likelihood of poor outcome increased with

  \[
  \text{Odds Ratio (Poor)} = 2.26 \ (1.24 \text{ -- } 4.12)
  \]

- Your odds of survival were 1:20, now 1:40

FYI: Powerball odds of winning (something) are 1:37
Effects of Hypothermia

- Second, it may decrease your vasopressor use!
- 10 pigs survived to 1 hour after arrest
- 5/6 pigs that did not require pressors were cooled

Norepinephrine (mcg/kg) after ROSC

<table>
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<tr>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
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Why?

- Decreasing temperature increases myocardial contractility
  - ↑ isometric twitch force in isolated muscle
  - ↑dP/dT, ↑ stroke volume in vivo
  - ↓ heart rate in vivo (like β-blockade)
  - ↑ cardiac output
  - No real change in SVR, PVR in this temp range
- Decreasing temperature may save myocardium

Hypothermia and the Injured Heart

- Mild hypothermia reduces ultimate infarct size.
  - LAD occlusions in 60-80 kg swine for 60 minutes
  - Endovascular cooling to 34°C from 20-75 minutes

Circ Physiol 282: H1584-1591
1. Temperature Monitor

Initial Temperature for OOHCA in Pittsburgh

Cranial

Core
2. Cooling Devices

Cold (refrigerator) IV Saline

30 ml/kg NS (~2 liters) administered to conscious volunteers over 30 minutes. Core temperature measured using wireless "pill thermometer".

Cold IV Saline + Shivering Suppression

Benzodiazepine enhanced cooling

Valium 10 - 20 mg
Brrr, that’s cold!

- Normal people will shiver and not cool more than 1 °C
- We can abate that with benzos or propofol
- Last resort is paralysis, but watch for seizures
- Cold IVF gets people cold faster, but you will need more than fluids to maintain.

Cooling blankets are available in essentially every ED and ICU.

Other Options

- NG Lavage with iced saline- D’Cruz method
- Cool Guard Catheter
  - 50k for machine
  - 1k for catheter
**Take Home on Devices**

- **Induction Phase**
  - Cold saline is best
  - NG Lavage may help
  - Cold packs if nothing else available

- **Maintenance Phase**
  - Blanket is cheap and effective
  - Catheter is sexy

**Just do it!**

- Cooling blankets, ice packs, Cool-Guard
- Catheter for maintenance

  - Keep them cool for 24 hours at 34°C
    - <24 may work as well

  - Then, gradually warm them: <1°C/hr

  - Watch for seizures!
    - Incidence of ~10%

**Perilous Side Effects?**

- Cardiovascular Effects
- Electrolytes and Fluid Shifts
- Bleeding
- Infection
- Side effects of cooling method
Blood Gases and Temperature

- When a patient is cooled, pCO₂, pO₂ decrease, and pH increases, measured at the patient's temperature.
  - \[ \Delta pCO₂ = 4.5\% / ^\circ C \]
  - \[ \Delta pH = -0.015 / ^\circ C \]

At 37°C in Machine: 7.35 / 45 / 100
At 33°C in Patient: 7.41 / 40 / 90

Blood Gases in Hypothermia

- pH-stat method: paCO₂ and pH are corrected for the patient's temperature.
- Alpha-stat method: paCO₂ and pH are measured at 37°C.
  - Easier (Just run the ABG and ignore temp)
  - In stroke, preserves normal brain autoregulation at mild to moderate hypothermia. (=mild hyperventilation) (Georgiadis, 2002, Stroke 33: 3026-9)
Take Home:

Just run the gas, and adjust the ventilator as you would in the normothermic patient.

Electrolyte and Fluid Shifts

- As you cool the patient, vasoconstriction will decrease effective vascular volume.
  - Diuresis
  - Lose potassium
  - Lose phosphate
- Potassium shifts intracellularly

(Abikri 2001; CCM 29: 1726-30; Zeiner 2004; Resuscitation 60: 253-61)

Electrolyte and Fluid Shifts

- As you warm up, patient intravascular space expands, and potassium shifts out of cells
  - Danger of hyperkalemia if you replaced potassium earlier
  - May appear volume depleted
**Hypothermia effects on blood**

- Fever is common after cardiac arrest
  - Pneumonitis develops in 25%
  - Some infection develops in 40-50%
- Infections increase with hypothermia > 24 hours
  - Macrophage / leucocyte function is slowed
  - Effect is minimal if hypothermia < 24 hours
- Bleeding increases below ~35°C
  - Clotting factor reactions are slowed
  - Caution if serious bleeding occurs

**HACA – Complications (all N.S. between groups)**

<table>
<thead>
<tr>
<th></th>
<th>Normothermia</th>
<th>Hypothermia</th>
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</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>19%</td>
<td>26%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>29%</td>
<td>37%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>7%</td>
<td>13%</td>
</tr>
<tr>
<td>Pulmonary Edema</td>
<td>4%</td>
<td>7%</td>
</tr>
<tr>
<td>Renal Failure / HD</td>
<td>10% / 4%</td>
<td>10% / 4%</td>
</tr>
<tr>
<td>Seizure</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Serious Arrhythmia</td>
<td>32%</td>
<td>36%</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>
Hypothermia after Trauma?
Wang 2005; CCM 33:1296-1301

• Hypothermia after trauma is associated with increased mortality
• All bleeding eventually... stops

3. Treat ACS

• Up to 80% have MI as etiology for CA

• 2 Recent Consults:
  - 33 M with 99% LAD and 70% Circumflex
  - 35 F with 100% RCA

• 12 lead ASAP
• Consider anticoagulation after CT Brain
• Not IF they need a cath, WHEN!

4. Pump them up!

• Many patients exhibit sepsis-like physiology

• Increased HR, decreased SVR and contractility

• Support it and things will improve!
After more than a few minutes of circulatory arrest, ROSC is followed by CRUMP.

You better be mixing up pressors here.

Dopamine

4. Pump them up!
- Dobutamine is my first choice
  - Many patients have myocardial stunning post arrest
  - This is transient and lasts <24 hours
- Consider Norepinephrine if necessary
- Shoot for MAP >80 mmHg

5. Control the Glucose
- Better outcome with moderate glucose control (80-140 mg/dl)
- Similar to Surgical ICU patients- NEJM
- Linear increase in myocardial infarct with glucose levels in blood
- Worse stroke outcomes with hyperglycemia
6. Rehab is key

• Many patients have subtle cognitive changes post-arrest

• “Look great from a galloping horse”
  - Eat + Poop + Walk = D/C
• If you rehab them, they regain function

• If not…

Take Home: Post-Resuscitation

• Induce mild hypothermia

• Treat acute coronary syndrome

• Watch for seizures

• Pump them up!

• Control glucose

Questions?
It is the WHOLE PACKAGE that Matters Most

Langhelle - 459 subjects in 4 cities in Norway

Variability in Outcome - Pittsburgh
The Whole Package

- It is possible to dramatically increase survival in a given system (31% to 56% of admitted patients surviving to one year)
- Unlikely that it is one particular intervention.
- More likely, it is the whole package of proactive critical care delivered with a sense of urgency.


*Protocol includes therapeutic hypothermia*

Hypothermia- Is it Used?

- National database (NRCPR)- 2%
- UPMC- Presby (IHCA- 2006)- 24%
- UPMC- Presby ED (OHCA 2006)- 76%
What do I do with this?

- Referral center for hypothermia
- Institute it locally
- Send them out
412-647-7000

Post-Cardiac Arrest Service

Provide the second hour of critical care for our ED partners
Help make a consistent plan of care on the inpatient side
Address common post-cardiac arrest pathophysiology
Follow on to the floor/rehab

Process

Print on Demand - CCM
Case Review: DK

- Brought to a Community Hospital and placed on a balloon pump
- Air medical crew began prehospital hypothermia approximately 2 hours post arrest
- Neuro exam upon arrival
  - Myoclonic jerking
  - 4mm pupils minimally reactive
  - Corneal reflex on right side
  - Gag reflex present

Case Review: DK

- Treatment Issues
  - Prolonged arrest
  - Potential head injury
  - Possible C-spine injury
  - Bleeding from facial lacerations
Case Review: DK

• Outcome
  - Extubated on day 4
  - Minor memory deficit
  - Minor executive function compromise
  - Beginning Neuro rehab
  - Awaiting CABG

Mechanism of Hypothermia

• Decrease in cerebral metabolism
  - 6% reduction for every 1°C drop in temperature

• Suppression of reperfusion injury
  - Decreased free radical production
  - Reduction in excitatory neurotransmitters
  - Suppression of Ca²⁺ mediated cell death
  - Anti-inflammatory effects

Nolan et al. (2003) Circulation

Is Early Better?

• Ischemic injury occurs in neuronal tissue within minutes.

• Reperfusion injury may begin within minutes and is followed by a period of hypoperfusion which persists for 12 hours or more.

• Reducing demand during periods of ischemia while mitigating reperfusion injury makes intuitive sense.
Is Early Better?

- Animal data suggest early induction of hypothermia improves outcome.
  - Stertz et al. (1991) Crit Care Med
  - Kuboyama et al. (1993) Crit Care Med

- No studies comparing early versus delayed hypothermia in humans.

Is Early Better?

- HACA patients required 4-16 hours to reach target temperature and still demonstrated benefit.

- Are there risks to early hypothermia without continued hospital cooling?
  - Increased incidence of hypothermia associated complications?
  - Neuro-protective benefit is nullified

Is Early Better?

- Abella and Suffoletto describe the use of hypothermia as infrequent. Prehospital induction of hypothermia may overcome institutional inertia.

- Prehospital hypothermia may allow medical directors to redirect post arrest patients to centers capable of delivering hypothermia and other potentially related services such as PTCA.
Is Early Better?

- Davis et al. recently suggested that diversion to Cardiac Arrest centers may be feasible as most patients are resuscitated in the field and there was no relationship between survival and transport time.

- Analogous to a Trauma Center. Most facilities can initiate care but the survival benefit depends on tertiary care elsewhere.

Is Early Feasible?

- Australians began cooling in the field using only ice packs and wet cloth.

- Early is feasible.
  - Kamarainen- 5 patients treated with 4 degree saline.
  - Kim-63 patients with cold saline.

Cold Saline in the Field?

Patients given 2 L of 4°C normal saline post-arrest.
Without cooling blanket, the patients re-warmed rapidly.
Is Hypothermia Safe for Prehospital Providers?

- Both large RCT's had highly selective populations.
  - Nolan et al. (2003) Circulation
  - Bernard et al. (2002) NEJM
  - HACA (2002) NEJM

- Mild hypothermia has not been associated with increased incidence of sepsis and bleeding.

- Hovdenes included hemodynamically unstable patients on pressers and IABP’s.

Is Hypothermia Safe for Prehospital Providers?

- Inclusion Criteria
  - ROSC
  - Age >18
  - GCS <8 or unable to follow verbal commands

Is Hypothermia Safe for Prehospital Providers?

- Exclusion Criteria
  - Pregnant
  - Environmental Hypothermia
  - Traumatic Arrest
  - Active Bleeding
  - Cardiac Instability
    - Refractory or recurrent dysrhythmia
    - Inability to maintain MAP>70 despite use of a vasopressor
What is the Best Method of Prehospital Cooling?

• Busch et al. demonstrated successful cooling in Norway with ice packs and towels.

• In controlled environments, ice packs and exposure reduce temperature by 0.1°C per hour.

• Forced air systems similar to HACA study cool at 0.3°C per hour.

• Bernard’s initial protocol relying on surface cooling decreased temperature by 0.9°C per hour.

• Catheter based systems may be more efficient but are invasive and require equipment not available to prehospital providers.
What is the Best Method of Prehospital Cooling?

• A combination of exposure and cold saline is effective and practical for prehospital providers.

• Bernard et al. demonstrated that the core temperature could be reduced 1.6°C using 30 ml/kg of 4°C saline in 30 min.

• Virkkunen et al. decreased core temperature by 1.9°C using 30 ml/kg of 4°C Lactated Ringers in an average of 27 min.

• Crystalloid fluids can be kept at 4°C in specialized coolers.
What Adjuncts are Useful for Cooling?

- Thermometer
  - For initial temperature
- Sedatives
  - For patient comfort and to prevent shivering
- Paralytics
  - May be required to prevent shivering
- Airway management
  - Most patients will require intubation or alternative airway use.

POST CARDIAC ARREST HYPOTHERMIA

- Criteria:
  - Patient with cardiac arrest and return of spontaneous circulation
  - GCS <8
  - No trauma or active bleed
  - No environmental hypothermia
• Protocol:
  1. Intubate per Airway protocol
  2. Establish IV/IO access
  3. Sedate the patient as per the sedation protocol
  4. Remove space blanket and any other coverings from the patient.
  5. Place ice packs in the axilla and groin.
  6. Infuse a bolus of 1 liter of cold saline as fast as possible using a pressure bag.
  7. If systolic blood pressure is less than 90, Initiate Levophed infusion at 1-10 micrograms/min [norepinephrine 2 milligrams/250 cc NSS] and titrate in increments of 5 micrograms/kilogram/min every 5 minutes until:
     - Systolic blood pressure of 90-100 mmHg
     - Improvement of tissue perfusion
     - Development of ventricular dysrhythmia
  8. Consider administration of dobutamine infusion at 5-20 micrograms/kilogram/min [dobutamine 500 milligrams/250 cc NSS]. Titrate per medical command.

• Inclusions:
  1. All patients with sustained ROSC > 5 minutes post cardiac arrest (defined as chest compressions or defibrillation performed) and:
     a. Unable to follow verbal commands if intubated
     b. Unable to open eyes and verbalize if not intubated

• Exclusions:
  1. Age < 18 y/o
  2. Traumatic cardiac arrest
  3. Significant head trauma
  4. Actual or suspected significant hemorrhage (GI bleeding, AAA, etc.)
  5. Suspected significant hypothermia already present
  6. Frank pulmonary edema
**Procedure:**
1. Notify command MD that post ROSC hypothermia protocol is being initiated
2. Obtain 2nd large bore IV or IO access if feasible
3. Pressure infuse one (1) liter of chilled NSS at maximum feasible rate
   a. Label bag with **hypothermia protocol** label
4. If SBP > 100 administer 10 mg Diazepam IVP, give an additional 5 mg q5 minutes x2 (Maximum total 20mg) as needed to suppress shivering
5. On arrival at receiving facility notify staff that the hypothermia protocol has been initiated

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**Delivering the Whole Package**

- On-call service since January 2007
- Formalized bedside care started in July 2007
- Available through UPMC MedCall
- Data are Jan-Nov 2007
  - All prehospital cardiac arrests reviewed for QA

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**Results to Date- OHCA**

- 31 total OHCA patients
- 26/27 eligible patients received hypothermia
  - 96% of OHCA patients!
Results to date- OHCA

- 31 total OHCA patients
- 26/27 patients received hypothermia - 96% of OHCA patients!
- Overall Survival: 47%

Results to Date- OHCA

- 31 total OHCA patients
- 26/27 eligible patients received hypothermia - 96% of OHCA patients!
- Overall survival: 47%
- Good outcome: 38%

Summary

- Hypothermia is part of a care package
- Prehospital hypothermia will not improve survival UNLESS
  - Hospitals continue therapy
  - Patients receive rehab and secondary prevention
- Transport to closest appropriate facility
- Feedback to EMS as part of CQI
Alternative Cooling

Advanced Cooling System

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References

References