The Cold Hard Facts:

THERAPEUTIC HYPOThERMIA IN CARDIAC ARREST
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Clinical Scenario

- On 5/6/2014 54yo male collapses while riding his skateboard at the beach.
- Off-duty ER Physician and bystanders perform ACLS on the patient for 14 minutes. AED is used to convert V-Fib.
- The patient is resuscitated, intubated and transferred to PLCMMCT where he is found to be unresponsive and having ASTE-MI.
- Transferred to cath lab and multiple stents placed
- Therapeutic Hypothermia protocol is started...
What’s old is new again
Therapeutic Hypothermia (TH): A Novel Treatment?

- Ancient Egypt: The Edwin Smith Papyrus, 1700 BC [1]
- “Russian resuscitation”: Covering Cardiac Arrest Patients in snow, 1803 [3]
- Temple Fay’s article on TH for Intractable Cancer Pain, 1939**[4]
- Beck and Bailey used TH in cardiac surgery, 1950’s[5]
- Williams: 2 studies Post-Arrest TH ROSC, 1958-59[6,7]
- AHA and ERC recommend TH with ROSC, 2002-2003
Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest

The Hypothermia after Cardiac Arrest Study Group

- The Study: Out-of-hospital cardiac arrest due to VF with ROSC but a high likelihood of anoxic brain injury
- 3551 pts assessed 275 pts enrolled, 138 normothermia, 137 TH
- Circulating cold air and ice packs used to reach 32-34°C
- Patients cooled over 8-12hrs and rewarmed over 48hrs
- Similar groups except more DM and CAD and bystander CPR in the normothermia group
- Favorable neurologic outcome 6mos: 39% NT vs 55% TH
- Death: 55% NT vs 41% TH [8]
Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia

- The Study: Out-of-Hospital Cardiac Arrest with ROSC from VF and Comatose
- 77 pts enrolled, 34 normothermia, 43 TH
- Cooling with Cold Packs to a core temp of 33°C
- TH Patients cooled for 12-18hrs then active rewarming for 6hrs
- Similar groups except TH had higher % of women and lower bystander performed CPR
- Favorable Neurologic Outcome: 26% NT vs 49% TH
- Death: 68% NT vs 51% TH [9]
Physiology Ahead
Physiologic affects of Circulatory Arrest

- Arrest: LOC >> isoelectric EEG >> Anaerobic glycolysis >> decreased energy stores >> cellular depolarization >> Ca^{2+} influx
Reperfusion established >> reperfusion leads to O2 free radicals >> NMDA receptors are activated >> IC Ca2+ rises even more >> Cell Death [10]
Physiologic effects of Hypothermia

- TH reduces cerebral metabolism, oxygen consumption, glucose utilization\[^{11}\]
- TH protects cell walls and lipoprotein bilayer.
- TH inhibits NMDA receptor activation
- TH improves O\textsubscript{2} supply and decreases IC Pressure. \[^{12}\]
Physiologic Effects of Hypothermia

- TH induction may decrease heart rate and an increase SVR
- TH reduces ventilation requirements [13]
- TH decreases cardiac output by 7% for each 1°C decrease [14]
- TH leads to increased diuresis [14]
- TH produces “pseudo” hypokalemia and hyperglycemia [15]
- TH inhibits platelet function and prolongs PT and PTT [16]
Effective Cooling Strategy
Cooling techniques

- Ice packs
- Caps or helmets
- Cooling blankets
- Hydrogel cooling pads (i.e. Arctic Sun) 1.4°C/hour \(^{[19]}\)
- Cold water immersion
- Cold IV fluids (4°C)
- NG, Peritoneal or rectal lavage\(^{[17]}\)
Cooling Technique Limitations

- Time to cooling is long: 2-8hrs with surface cooling \cite{18}
- Higher cost (System: $54,000, Pads: )
- Shivering
- Tight temperature control is difficult
- Internal cooling devices are cumbersome and invasive.
- Out-of-hospital cold IV fluids, several studies show feasibility but outcomes not improved compared to ED cooling \cite{20}
- Physiologic side effects of TH.
- High resource demand for additional monitoring/nursing.
Temperature Monitoring
Temperature Monitoring

- Must be reliable, constant and easy to place
- PLCMMCT uses Foley Catheter bladder probes
- PA Catheter is most accurate\[21\]
- Rectal
- Vaginal
- Tympanic
- Esophageal
Timing and Duration of TH

- The earlier the better after ROSC \[^{18}\]
- Systematic Literature Review for prehospital TH yielded 11 studies with poor quality in 8 and big differences in methodology \[^{22}\]
- Duration: Unclear
- ILCOR suggest TH for 12-24hrs\[^{18}\]
- Longer cooling for potentially reversible intracranial HTN.
Rewarming

- Rewarming not to proceed faster than 0.5°C to avoid overshoot
- Why not as quick as possible?
- Leary et al, retrospective review, 11 hospitals, 2005-11
- Looked at rebound pyrexia (>38°C)
- 236 post-arrest patients, 41% had rebound pyrexia
- No difference on survival and neurologic outcomes with mild pyrexia 38.7°C
- However >38.7°C, 58% vs 80% had worse neurologic outcomes[23]
Potential Complications

- **Shivering:** Demerol, Paralytics, Propofol
- **Hypotension:** Control with Fluids and Pressors
- **Sedation:** Propofol or Midazolam
- **Electrolytes:** Control Hypokalemia/Hypophosphatemia and hypomagnesemia, Hyperglycemia
- **Bleeding:** Monitor potential bleeding sites and PT/PTT/INRs
- **Infection:** Watch for pneumonias and low WBC counts.
- **VTE:** Prophylaxis per protocol.
Exclusion Criteria UPenn

- >12hrs since ROSC
- Glasgow Motor score >5
- Minimal pre-morbid cognitive status
- Other reasons for coma (ICH, CVA, Sedation)
- Sepsis as etiology for arrest
- DNR or DNI
- Uncontrollable bleeding
- Significant trauma (Liver or spleen Laceration)
Inclusion Criteria
PLCMMCT

- Resuscitated post out-of-hospital or in hospital witnessed VF, VT cardiac arrest or PEA
- ROSC<60 minutes after arrest
- Unresponsive following cardiac arrest
- Stable hemodynamics with or without vasopressors or IABP. Vasopressors not at max doses and SBP > 90 after 60min of resuscitation.
- Patients must meet all criteria to be eligible for TH.
Absolute Exclusion Criteria
PLCMMCT

- Unknown downtime
- DNR and/or DNI, Do not attempt CPR
- Pregnancy
- Sustained hypotension (SBP <80mmhg or Map < 50mmhg) > 60min despite vasopressors
- Patients <17 or >85yo
- Sustained refractory ventricular arrhythmias
- Clinical suspicion of head or chest trauma
- Known Bleeding diathesis or active bleeding
- Severe Bradycardia, Terminal Illness, Initial temp <34° C
Relative Exclusion Criteria PLCMMCT

- Chronic Renal Failure
- Chronic Liver Failure
- Patients on Warfarin (Consider Reversal)
- Platelets <50,000
- Drug intoxication known to cause CNS depression (opiates, BDZ, Lithium, Antiepileptics)
# Therapeutic Hypothermia Basics

<table>
<thead>
<tr>
<th>Ideal Candidate</th>
<th>Cardiac Arrest with rapid ROSC, VF/VT, hemodynamically stable, unresponsive</th>
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<tbody>
<tr>
<td>How Soon?</td>
<td>ASAP, May still benefit 8h post ROSC</td>
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<tr>
<td>How to Induce?</td>
<td>Arctic Sun, Ice packs to groin, axilla, and neck Adjuncts-cold saline boluses, Cooling blankets, Fan Mist</td>
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<tr>
<td>Adjunctive Medications</td>
<td>Sedation, Pressors, Paralytics</td>
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<tr>
<td>Temperature Measurement</td>
<td>Continuously Monitored Bladder, Esophageal, PA or rectal temps [24]</td>
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Questions still to be answered

- The ideal method of cooling
- The timing and duration of cooling
- The timing and duration or rewarming
- The use of TH in non-shockable rhythms
- The use of TH with in-hospital cardiac arrest
- The use of TH in other disease entities such as CVA, TBI, Hepatic Encephalopathy and ARDS.\[25, 26, 27, 28\]
The hypothermia protocol is carried out.

The patient wakes up and continues recovery over an 8 day hospital stay.

On post-arrest day 8 the patient is discharged from PLCMMCT in good condition with new stents, no residual neurological effects and most importantly...a second chance.
References

References


