Targeted Temperature Management

Where are We Today?

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Disclosures

• Currently employment: Clinical Nurse Specialist/Clinical Practice Manager at North Bay Healthcare System Fairfield, California

• Past AACN Board Member

• No Financial Incentives or Honorariums to report:
  • Referred to Contra Costa Chapter By Arctic Sun Representative
Objectives

By the end of the session the participant will be able to:

• Discuss the evidence to date related to therapeutic temperature management for the post-cardiac arrest patient.
• Identify the pros and cons of both TTM to 36 degrees vs 33 degrees.
• Review the different methodologies/devices used for TTM
• Describe potential complications of TTM and appropriate anticipatory interventions and troubleshooting to implement as they occur.
Out of Hospital Cardiac Arrest Facts

- Sixty-seven studies from Europe, North America, Asia or Australia
- Utstein (1991) data reporting guidelines—compare incidences per 100,000 person-years of attending OHCAs

<table>
<thead>
<tr>
<th>Percentage of Out-of Hospital Arrests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidences per 100,00 person years</td>
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<table>
<thead>
<tr>
<th>Region</th>
<th>Incident of treated OHCA</th>
<th>Percent of VFib</th>
<th>Survival to Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>54.6%</td>
<td>28%</td>
<td>6%</td>
</tr>
<tr>
<td>Australia</td>
<td>44%</td>
<td>40%</td>
<td>11%</td>
</tr>
<tr>
<td>Europe</td>
<td>35%</td>
<td>35%</td>
<td>9%</td>
</tr>
<tr>
<td>Asia</td>
<td>28.3%</td>
<td>11%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Resuscitation, 2010 Nov, 81(11) 1479-87 Epub 2010 Sep 9
Out-Of-Hospital Cardiac Arrest (OHCA)

- Worldwide, >135 million cardiovascular deaths occur each year.
- Globally, the incidence of OHCA is 20-140 per 100,000 people with survival from 2%-11%
- In the United States, > 500,000 children and adults OHCA with 88% occur in the home
  - <15% survive

*Cardiac Arrest is one of the most lethal public health problems in the United States*
Cardiopulmonary Resuscitation – CPR

- Survival is directly linked to the amount of time between the onset of cardiac arrest (V Fib) and defibrillation
- Less than 1/3 of OHCA sudden cardiac arrest victims receive bystander CPR
- Immediate effective bystander CPR can double the chance of survival
In Hospital Cardiac Arrest Facts

- Values range between 1 and 5 events per 1,000 hospital admissions
- Reported survival to hospital discharge varies from 0% to 42%, the most common range being between 15% to 20%
- In Hospitals participating with the Get with the Guidelines-Resuscitation quality improvement program:
  - Adult cardiac arrest survival rate: 18% (range 12%-20%)
  - Between 7AM to 11 PM survival is > 20%
  - Between 11 PM to 7 AM only 15%
  - Unmonitored units at night – 9% survival
In-Hospital Factors Influencing Outcomes

- Lack of implementation of therapeutic hypothermia and temperature management
- Missing standard operating procedures/protocols for post-resuscitation care
- Time lapse from ROSC to start of interventional phase
- Training and experience of personnel
- Inadequate post-arrest treatment decisions
Best Chances for Survival

CPR INSTRUCTIONS

STEP 1: CALL 911
STEP 2: APPLY CHEST COMPRESSION 100 PER MINUTE

PUSH HERE

*These are instructions for hands-only CPR. If you are trained in regular CPR, then proceed as trained.
Where did Hypothermia Come From?
History

• Induced hypothermia researched in late 1950’s but was abandoned due to
  • Questionable benefits
  • Adverse reactions
  • Difficulties inducing
  • Maintaining hypothermia
History

- Achieving hypothermia took several hours
- Trialed with TBI and Cardiac Surgery
- Amount of sedation and anesthetic to treat shivering unsafe for patient
  - Respiratory depression
  - Hypotension
  - Infection
  - Ventricular arrhythmias
  - Coagulopathies
History

- Revisited in 1980s-1990s in small safety and feasibility clinical trials in animals and human subjects
  - Better outcomes
  - Less adverse reactions
    Due to improved management of adverse reactions & better equipped ICUs
- Still research mostly focused on attempts to improve short-term survival
Cooling to 34-32°C for 24 hours in comatose survivors resulted in an impressive improvement in neurologic outcomes (55%) and overall survival versus 39% of normothermic control group.

- Mortality at 6 months:
  - Hypothermia 57/137 (41%)
  - Normothermia 76/138 (55%)

- Complications:
  - Not significant between the two groups
Landmark Clinical Studies

Idrissa:

• Alive at hospital discharge with favorable neurological recovery

• Alive at 6 months with favorable neurological recovery
  • Hypothermia 4/16 (25%)
  • Normothermia 1/17 (6%)
Landmark Clinical Studies

- Australian Researchers: Bernard et al.
  - Good neurological outcomes in 21/43 (49%) of the patients versus 9/34 (26%) in control group
## Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Multicenter</th>
<th>Main Site</th>
<th>Patient Rhythm</th>
<th>Patient Location</th>
<th>N</th>
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<tbody>
<tr>
<td>HACA</td>
<td>Yes</td>
<td>Austria</td>
<td>VF</td>
<td>OHCA</td>
</tr>
<tr>
<td>Bernard</td>
<td>Yes</td>
<td>Australia</td>
<td>VF</td>
<td>OHCA</td>
</tr>
<tr>
<td>Idrissi</td>
<td>No</td>
<td>Belgium</td>
<td>PEA/Asystole</td>
<td>OHCA</td>
</tr>
</tbody>
</table>
HACA Study

~37.6°C

Graph showing temperature changes over time after restoration of spontaneous circulation, with data points for normothermia and hypothermia.
Hypothermia Research

- Six studies with historical control groups reported a beneficial effect on outcome from use of therapeutic hypothermia in comatose survivors of OHCA associated with any arrest rhythm
  - Sunde, K et al (2007)
In-Hospital Cardiac Arrests

Therapeutic hypothermia reduces death

• Mayo researchers analyzed a database covering more than 1 million patients

• Mortality rates among in-hospital sudden cardiac arrest patients
  • 2001 = 69.6% (Pre study published)
  • 2009 = 57.8% (Post study published)

12% reduction in deaths
Hypothermia in the News
Hypothermia in the News

• Newsweek Cover story on Hypothermia... May 2007
  • Bill Bondar, 61 yr old retired computer programmer – cardiac arrest while unloading his car.
  • Wife, Monica, began CPR, called 911, Paramedics arrived – 2 shocks delivered, taken to local community hospital.
  • “Stabilized cardiac but now in a coma”
  • Monica asked for him to be transferred to 15 miles away to Penn.
Buffalo Bills player: Kevin Everett treated with Hypothermia

“I was trying to pull out all the stops to help this young man,” Cappuccino said Wednesday at a news conference. He had heard of the therapy called, Moderate hypothermia, at a conference attended by doctors from Miami Project to Cure Paralysis who have been experimenting with it for more than a decade.

September 14, 2007
Hypothermia in the News

Popular Science
February 2009

“Cold Relief: Two Philadelphia Doctors are Championing an Unconventional New Treatment for Keeping Cardiac-Arrest Victims Alive, With as little Brain Damage as Possible: Just Give them Hypothermia”

- Pam Barco, 46 yo Children’s Hospital of Philadelphia, ED Clerk collapsed at work; defibrillated twice, when stable – moved next door to Penn.
When to use Hypothermia

Other Rhythms?

- One study reported better neurological outcomes after V Fib cardiac arrest but not with other rhythms (2009)
- Two non-randomized studies found possible benefit with hypothermia in non-Vfib cardiac arrests (2006 & 2007)

Timing?

- Some studies start within 2 hours of arrest and at target by 8 hours (2004)
- Others timing of cooling and at target not associated with improved neurological outcome (2009)

How Long?

- At least 12 hours and maybe > 24 hours (2002)
- Longer duration of cooling has been studied in neonates but not on adults (2005)
Post-Cardiac Arrest Care 2010/2013

“For protection of the brain and other organs, hypothermia is helpful therapeutic approach in patients who remain comatose, usually defined as lack of meaningful response to verbal commands, after ROSC.”
Change in Recommendations

American Heart Association 2010:

- Evidence Based Guidelines
  - Mild to Moderate Hypothermia: Adult patients with ROSC after Out-of-Hospital V Fib Cardiac Arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12-24 hours (Class I, LOE B)

- Consider hypothermia for comatose adult patients with ROSC after in-hospital cardiac arrest or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIb, LOE B)

- Active rewarming should be avoided in comatose patients who spontaneously develop a mild degree of hypothermia (> 32°C [89.6°F]) after resuscitation from cardiac arrest during the first 48 hours after ROSC (Class III, LOE C)

Peberdy et al. 2010
European Study: Therapeutic Hypothermia

- European Study Mortality: decreased by 20%
- OHCA Outcomes – Randomized and non-randomized studies
  - Initial rhythm of VT/VF 50% survival
- Analysis of Cost Effectiveness in the United States
  - Post-arrest patients gained an average of 0.66 quality adjusted life years compared with conventional care

Van der Wal, et al 2011
Targeted Temperature Management

- Targeted Temperature Management aims to mitigate a cascade of secondary injury mechanisms, which started immediately after the initial event (primary injury) and may last for hours /days.

- This contributes to neurological morbidity and/or mortality of patients.
Targeted Temperature Management

• Two forms of Target Temperature Management (TTM)
  • Therapeutic Hypothermia: Internal reduction of a patient’s core temperature below 36.0° C (32° C through 35° C)
  • Controlled Normothermia: Bringing down core temperature in a patient with fever, and maintaining temperature within a range of 36.0° C through 37.5° C
Definition and Levels of Hypothermia

Hypothermia: Core temperature below 36.0°C regardless of the causes

Induced Hypothermia: An intentional reduction of a patient’s core temperature below 36.0°C

TTM: Why Do We Cool?

- Decrease intracranial pressure (ICP) in patients with traumatic brain injury or ischemic stroke

- Mitigate myocardial injury following myocardial infarction

- Reduce the inflammatory response in ARDS and in numerous other situations

Poldeman 2008
TTM: Who Do We Cool?

• Therapeutic hypothermia has been most convincingly demonstrated in two categories of patients with global post-ischemic brain injury

• Level I Evidence
  • Post-anoxic injury (post cardiac arrest)
    • Patients with cardiac arrest with post-anoxic encephalopathy (Two randomized trials and more than twenty non-randomized studies)
  • Newborn asphyxia
    • Newborn babies with neonatal asphyxia (5 multi-center randomized control trials)
TTM: Who Do We Cool?

- Level I-IV Evidence
  - Refractory Increased ICP r/t
    - Traumatic brain injury
    - Ischemic stroke
    - Intracranial hemorrhage
  - Ischemia secondary to vasospasm in aneurysmal subarachnoid hemorrhage
  - Super refractory status epilepticus
Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

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David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sc.,
Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D.,
Jesper Kjaergaard, M.D., D.M.Sc., Michael Kuiper, M.D., Ph.D., Tommaso Pellis, M.D.,
Pascal Stammet, M.D., Michael Wanscher, M.D., Ph.D., Matt P. Wise, M.D., D.Phil.,
Anders Åneman, M.D., Ph.D., Nawaf Al-Subaie, M.D.,
Søren Boesgaard, M.D., D.M.Sc., John Bro-Jeppesen, M.D., Isolde Brunetti, M.D.,
Jan Frederik Bugge, M.D., Ph.D., Christopher D. Hingston, M.D.,
Nicole P. Juffermans, M.D., Ph.D., Matty Koopmans, R.N., M.Sc.,
Lars Kober, M.D., D.M.Sc., Jørund Langørgen, M.D., Gisela Lilja, O.T.,
Jacob Eifer Møller, M.D., D.M.Sc., Malin Rundgren, M.D., Ph.D.,
Christian Rylander, M.D., Ph.D., Ondrej Smid, M.D., Christophe Wener, M.D.,
Per Winkel, M.D., D.M.Sc., and Hans Friberg, M.D., Ph.D.,
for the TTM Trial Investigators*
TTM Trial 2010-2013

• 950 patients randomized
• 36 hospitals
• 10 countries
• Europe & Australia
Characteristics of the Population

- Witnessed Cardiac Arrest
  - 33° group 420 (89%)
  - 36° group 418 (90%)
- Bystander performed CPR
  - 33° group 344 (73%)
  - 36° group 339 (73%)
- Start of basic life support
  - Median 1 min both groups
  - Range 0-2 min
- Start ACLS
  - 33° group 10 min (6-13)
  - 36° group 9 min (5-13)
Inclusion Trial Criteria:

- Age ≥ 18 years
- Out of Hospital Arrest of presumed cardiac cause
- Sustained ROSC
- Unconsciousness (GS < 8): patients not able to obey verbal commands after sustained ROSC
Exclusion Trial Criteria

- Obvious or suspected pregnancy
- Known bleeding diathesis (medically induced coagulopathy [e.g. warfarin, clopidogrel] does not exclude the patient)
- Suspected or confirmed acute intracranial bleeding
- Suspected or confirmed acute stroke
- Unwitnessed cardiac arrest within initial rhythm asystole
- Known limitations in therapy and DNR order
- Known disease making 180 days survival unlikely
- Known pre-arrest Cerebral Performance Category 3 or 4
- > 4 hours (240 minutes) from ROSC to screening
- Systolic blood pressure < 8- mm Hg in spite of fluid loading and/or inotropic medication/intra aortic balloon pump
- Temperature on admission < 30° C
Methods

• Hypothermia Treatment Delivered
  • 24% endovascular
  • 76% surface cooling

• Treatment Groups
  • 33 degree: 476 patients
    • 16 patients rewarmed prior to the 28 hour time mark (time point of initiation of rewarming)
    • 132 patients treatment withdrawn
  • 36 degree: 433 patients
    • 115 patients treatment withdrawn
A difference between our trial and earlier trials\textsuperscript{2,3} is that we did not allow the natural trajectory of temperature evolution in either group; we actively controlled the temperature during the intervention period and aimed to prevent fever during the first 3 days after cardiac arrest. We enrolled patients with out-of-hospital arrests of presumed cardiac cause, in line with enrollment in earlier trials, but our sample was larger and we had fewer exclusion criteria, with approximately 20% of participants having nonshockable rhythms. Other
Current Use of Therapeutic Hypothermia
So Do We Compare the Trials?

How can this be?
Large Differences in Maintenance Temperatures

Nielsen et al. 2013

HACA Study 2002

Bernard et al; ≈ 37.3 °C

Normothermia (n=124)

Hypothermia (n=123)

~37.6°C

~36.0°C
Most Important point .......

Current work does not test the same hypothesis as the HACA, Bernard trials.

36°C arm in the trial is still active management of temperature.
Interpreting the Evidence

Degree of post-arrest injury

- **severe**
  - Poor outcome with any TTM

- **moderate**
  - Dose of TTM (33°C vs 36°C)
    - Affects outcome

- **Mild/None**
  - Good outcome with any TTM
Therapeutic hypothermia application vs standard support care in post resuscitated out-of-hospital cardiac arrest patients

Chieh-Jen Wang MD,*, Sheng-Hsiung Yang MD, Chiao-Hsien Lee MD, Rong-Luh Lin MD, Ming-Jen Peng MD, Chien-Liang Wu MD

Methods: A total of 175 OHCA patients underwent therapeutic hypothermia (TH), which was performed using large volume ice crystalloid fluid (LVICF) infusions after ICU admission. Ice packs and conventional cooling blankets were used to maintain a core body temperature of 33°C, according to standard protocol for 36 hours. Patients in the control group received standard supportive care without TH. Hospital survival and neurologic outcomes were compared.

Results: There was no significant difference between the groups with regards to patient characteristics, underlying etiologies, and length of hospital stays. The duration of cardiac pulmonary resuscitation (CPR) was also similar.
OHCA cases:

- Non-Therapeutic Hypothermia Group
  - 1.7% (2/124) had good neurologic outcomes
  - 27.5% alive at discharge

- Therapeutic Hypothermia Group
  - 7.9% (4/47) had good neurologic outcomes
  - 12.1% alive at discharge
Rationale for TTM Approach

Given that:

1. TTM trial was neutral (no difference in benefit or harm)
2. Cooling to 33°C is based on extensive laboratory evidence and two RCTs (HACA, 202; Bernard et al, 2002)
3. We can’t tell who will have significant post-arrest injury based on current technology and clinical factors
4. The chance to modify neurologic injury is in the acute care of post-arrest patients – and we don’t get a second chance
Recommended Approach

Therefore:

It is reasonable to not change current practice based on the TTM trial, but rather continue to treat comatose post-arrest patients with a TTM goal temperature of 33°C.

However, the TTM trial provides evidence that a more flexible approach is possible – for patients intolerant of 33°C: marked bradycardia, increased bleeding, marked QT prolongation …

Or for patients that clinicians feel uncomfortable with treating to 33°C for other clinical factors, it is acceptable to treat with higher TTM temperature goals, up to 36°C.

Abella, November 2013
Recommended Approach

• All comatose post-arrest patients should at least receive TTM with a maximum temperature goal of 36°C “normothermia” as defined by lack of any temperature control is not supported by the growing body of literature.

• In addition to TTM management in the acute phase (12-24 hours of either 33°C or 36°C TTM), arrest care, including aggressive avoidance of care withdrawal for at least 72 hours post arrest, as supported in the current AHA guidelines and the TTM trial.
The Brain at Risk: Initial Anoxic Event & Reperfusion Injury
Development of Ischemic Brain Edema

- Ischemic brain edema is a combination of two major types of edema:
  - Cytotoxic (cellular): edema evolves over minutes to hours and may be reversible
  - Vasogenic: occurs over hours to days and is considered an irreversible damaging process
Formation & Consequences of Edema

- Direct neuronal disruption and cellular injury
  - Cytotoxic edema
- Injury to the blood-brain barrier leading to increased permeability
  - Vasogenic edema
- Ischemia/reperfusion
- Hyperemia
- Local haematoma formation with local edema
- Increase in CSF volume (due to blocking of ventricular drainage)
- Increased cerebral blood volume

Intracranial hypertension
Pathology of Global Ischemia

Cardiac Arrest → inadequate oxygen and glucose which limit ATP production
• Ion pumps fail
  • Efflux of potassium out of the cell
  • Influx of sodium and calcium into the cell
• Resulting in cellular edema and terminal depolarization and cellular death
Brain at Risk of Ischemia

• Cells are exposed to ischemia can either become
  • Necrotic
  • Partially or fully necrotic, recover
  • Enter a path leading to programmed cell death (apoptosis)
• This process occurs over a period of minutes to many days after injury
Necrosis:

- Characterized by cell swelling and membrane rupture allowing the contents of the cell to leak into the surrounding tissue.
Apoptosis: Cell death by suicide

- Programmed cell death
- Following brief ischemic episode apoptosis usually prevails as the dominate cause of cell death in injured cells
How Does Mild Hypothermia Help

• Lowers metabolic rate (5-7% per 1 degree Celsius)
• Decrease in cellular demand for oxygen & consumption
  • Especially in highly aerobic organs such as brain tissue
• Decrease in carbon dioxide production
• Decrease in Cerebral Blood Flow
How Does Mild Hypothermia Help

- Stabilizes the cell membrane:
  - Decreases reperfusion injury and free radical oxygen production
  - Suppresses inflammatory reactions and inhibition of the release of pro-inflammatory cytokines
  - Inhibits neutrophil and macrophage function
Anoxic Injury - Warm

Cells consume oxygen and glucose to produce the energy molecule ATP.

Cells ion pump shuts down.

The cell immediately begins hoarding excess calcium ions and dangerous free radicals.

Disrupted ion levels provoke the immune system to attack the cell.

Mechanism inside the cell kick-start various processes that cause it to rip itself apart - suicide.
Anoxic Injury - Cold

Calcium levels and cell’s free radical remain relatively low

Maintaining normal ion levels in the cell does not alert the immune system to activate when the oxygen returns

The chilled cell is able to withstand the shock of restarting cellular metabolism and it recovers function
Hypothermia Neuroprotection?

Destructive processes following ischemia/reperfusion that can be prevented or significantly mitigated by hypothermia.

Black lettering = early mechanisms
Gray lettering = late mechanisms

Figure 1. Schematic depiction of the mechanisms underlying the protective effects of mild to moderate hypothermia. TxA2, thromboxane A2.

(Crit Care Med 2009; 37[Suppl.]:S186–S202)
How to Cool A Patient
Methods to Induce Cooling

- Inefficient Methods
  - Wet towels
  - Alcohol baths
  - Ice bags – labor intensive

- Surface cooling, air
  - Exposure of skin
  - Skin exposure combined with water or alcohol sprays or sponge baths
  - Air circulating cooling blankets
  - Fans
Methods for Controlled Induction of Hypothermia

- Surface cooling, fluids
  - Complete immersion in cold water
  - Circulating cold water directly against skin
  - Pre-refrigerated cooling/surface pads
  - Water circulating cooling blanket/pads
  - Hydrogel coated water-circulating pads/garments
  - Cooling helmets
Methods to Induce Cooling
Artic Sun 5000
Temperature Management System
Methods to Induce Cooling

- Core Cooling
  - Intravascular catheter
  - Iced NS IV (30 mL/kg) at 4°C
  - Peritoneal Lavage
Zoll Thermogard
Temperature Management System
Cold IV Fluids

**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

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

<table>
<thead>
<tr>
<th>Medications, mg/hr</th>
<th>Before Cooling</th>
<th>During Cooling</th>
<th>p Value</th>
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<tbody>
<tr>
<td>Dopamine, n = 54</td>
<td>17.4 ± 12.0</td>
<td>10.2 ± 9.2</td>
<td>&lt;.01</td>
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<tr>
<td>Norepinephrine, n = 56</td>
<td>0.42 ± 0.24</td>
<td>0.22 ± 0.18</td>
<td>.01</td>
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<tr>
<td>Dobutamine, n = 24</td>
<td>34.1 ± 32.2</td>
<td>32.2 ± 41.3</td>
<td>NS</td>
</tr>
<tr>
<td>Enoximone, n = 22</td>
<td>3.2 ± 3.6</td>
<td>3.0 ± 3.0</td>
<td>.13</td>
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Methods to Induce Cooling
Internal Cooling Devices

- Cooling catheter related concerns:
  - Initiation/insertion delays
  - Large femoral catheters (8.5 FR – 14.0 FR) that have caused documented DVT’s
- Catheter related concerns
  - Bleeding at insertion site
  - Infection
  - Clots
- Requires use of femoral vein which may compete for optimal location cardiac catheterization

1. Arrich, Resuscitation 2007 ERC Registry
2. Simosa, American Surgeon 2007
Caution with Cold IV Fluids

- Can be used for induction of hypothermia
- If not followed by another “hypothermia treatment method”
  - Can result in shivering
  - Can result in rebound rewarming
  - Use caution infusing into central line could result in VFib
Time to Treat

• Study by Neilson & Friberg (2009) suggests there is no relationship between time to target temperature and outcome
  • Goal temperature 34 C
  • Median time 260 mins
  • Range 178-400 minutes

• INTCAR database
  • Delay in initiation of Hypothermia and reaching target temperature
  • Poor neurological outcome ↑ for every 30 minutes delay in time to target temperature
  • 20% increase in the risk of death for every hour of delay to initiation of cooling

Neilson et al. (2009) Acta Anesthesiol Scand. 53

Mooney, MR et al. (2011) Circulation 124; 206-214
Case Study 1

- 63 yo male at home watching TV when his room mate noticed him gurgle and lose consciousness. He started CPR and called EMS.
- A perfusing rhythm was obtained in 15 mins, but there were repeated episodes of VF requiring multiple defibrillations and repeated episodes of CPR
- With ROSC, he was not responsive
- Initial ECG revealed inferior ST-segment elevation
- In ED, more defibrillation done then taken for PCI
- EMS started iced saline IV and ice packs were placed in ED and Cath Lab.
- Stent placed in Right Coronary Artery
- To ICU, surface cooling device placed and treated with Therapeutic Hypothermia for 24 hours, then re-warmed.
- He was initially comatose but by day 5, he was awake, alert and interactive.
- Soon he was discharged home
Case Study 2

- 54 yo female found down unresponsive by co-workers.
- Not clear how long she was down, CPR started and AED applied = no shock recommended
- EMS identified asystole as the initial rhythm
- After 25 mins of ACLS, a perfusing rhythm was obtained
- ECG showed no ischemic changes
- Patient unresponsive on arrival at ED
- CT Scan of head and pulmonary arteries normal
- Treated with Therapeutic Hypothermia for 24 hours, then rewarmed
- No change in Neuro status by day 5
- MRI did not reveal any major abnormalities, but incomplete recovery of brain stem reflexes and absent bilaterally Sensory Stimulatory Evoked Potentials
- Discussion with family members, continued treatment withdrawn and she expired
Neuroprognostication Time to Arousal

Studies support Both Beliefs:

• **Chandra-Strobos** “A Paradigm Redefined: Time Course of Neurological Recovery Following Hypothermia Therapy Post Non-Traumatic Out-of-Hospital Cardiac Arrest” Patient population: 47 patients with out-of-hospital arrests; 15 treated with TH (57% with VF as initial rhythm)

• Findings: Meaningful awakening can occur 7+ days post arrest in patients treated with TH

• **Mayo Neurology paper** Patient population: 227 patients with out of hospital arrests; 128 treated with TH (88% with VF as initial rhythm)

• Findings: Hypothermia does not delay time to arousal past 72 hours post-arrest
Neuro Assessment

• American Academy of Neurology neuroprognostication guidelines for comatose SCA patients
  • Detailed neurological exam at 72 hours after arrest
    • Myoclonic status epilepticus
    • Serum neuron-specific enolase (NSE) – biomarker for TBI
    • Somatosensory evoked potential (SSEP)
    • Pupillary light response
    • Corneal reflexes
    • Motor responses

Methods

Inclusion Criteria:
- Patients had a cardiac arrest (any initial rhythm) with ROSC and received therapeutic hypothermia between 2005-2011
- 3 Hospitals Cohort:
  - Hospital of the University of Pennsylvania
  - Penn Presbyterian Medical Center
  - Pennsylvania Hospital

Exclusion Criteria:
- Traumatic arrests
- < 18 years of age

Definition of Regaining Arousal:
- Purposeful movement
- Measured by a patient’s first recorded Glasgow Motor Score of 6 or a chart notation of purposefully following commands

Definition of Neuro Outcome:
- return to neurologic baseline (pre-arrest) or GCS 14-15

Grossestreuer, AV et al (2011) AHA
Hypothermia Protocol

• Temperature management was provided using a surface cooling device; most patients also received chilled saline and/or ice bags

• Target temperature, 33°C (with an acceptable range of 32-34°C), was maintained for 24 hours

• Rewarming, at 0.33°C/hour, was done actively using a surface cooling device
Results: Patients Waking at Day 7-8

- **Time to Arousal by Neurologic Outcome at Discharge**
  - X-axis: Days Post-Arrest
  - Y-axis: Number of Patients
  - Bars: Neurologically Intact (blue), Not Neurologically Intact (red)

- **Days to Arousal**
  - X-axis: Days Post-Arrest
  - Y-axis: Number of Patients
  - Bars: Survived to Discharge (blue), Did Not Survive to Discharge (red)
Neurologically Intact
Frankenstein’s Neuro Assessment
Thank you!

QUESTIONS??