

New Term

Targeted Temperature Management (TTM)

"...adopted to refer to induced hypothermia as well as to active control of temperature at any target."



Callaway et al. (2015). p. S467

Objectives

- At the completion of this session, the participant will
 - Briefly discuss the evolution of therapeutic hypothermia and the science underlying the therapy
 - Discuss the indications for use
 - Describe the process of therapeutic cooling: When and how?



Therapeutic Hypothermia Outline

- Case presentation
- Background
- Summary of current recommendations
- Overview of CJW Medical Center hypothermia protocol
- Case Studies



Case Study

- 41 yo black male with hx of HD, EF 20%, a. fib, pacemaker, CKD (hemodialysis)
- Calls EMS with c/o palpitations. During the call, the patient goes into cardiac arrest. Family begins CPR.
- EMS on scene within 5 minutes of initial call. Pt found pulseless with agonal gasps.
- Airway partially obstructed with emesis
- Initial rhythm ventricular fibrillation

Case Study

- Autopulse
- IO
- Defibrillation x9
- Vasopressin x2; epi x2
- Amiodarone bolus: 300mg; 150mg x2
- Calcium Chloride
- Sodium bicarbonate
- Intubation
- Capnography



Case Study

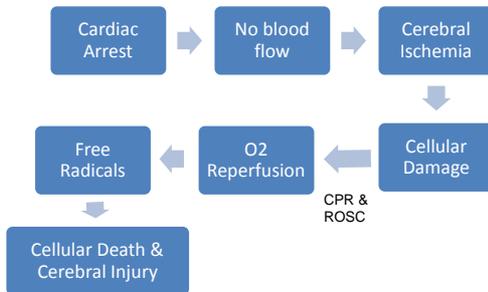
- ROSC upon arrival to ED; unresponsive
- TTM 34°C
- Fractured ribs
- Extubated, Day 3
- Subcutaneous ICD placed, Day 12
- Discharged neurologically intact, Day 14

Out-of-Hospital Cardiac Arrest (OHCA)

- Out-of-hospital cardiac arrest claims 236,000 – 325,000 lives each year in the United States
- Survival rates range from 0 - 11% depending on presenting rhythm
 - 3-7% of survivors returning to previous level of functioning
 - 19-32% of survivors have poor neurological outcomes
- Even when resuscitation efforts are successful, recovery is often limited by anoxic encephalopathy

Keonig et al (2008). *Neurologic Clinics*
Lundbye et al (2012). *Resuscitation*

Cardiac Arrest



Seminal Studies

The New England Journal of Medicine

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MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC
OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

- **Results:**
 - 75 of 136 patients treated with hypothermia (55%) survived to discharge with good neurologic outcome as compared to 54 of 137 treated with normothermia (39%)
- **Conclusion:**
 - Suggests that treatment with moderate hypothermia increases rate of favorable neurologic outcome & decreases mortality

INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

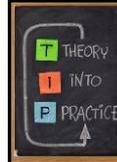
STEPHEN A. BERNARD, M.B., B.S., TIMOTHY W. GRAY, M.B., B.S., MICHAEL D. BUST, M.B., B.S.,
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TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

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- **Results**
 - 21 of 43 patients treated with hypothermia (49%) survived to discharge with good neurologic outcome as compared to 9 of 34 treated with normothermia (26%)
- **Conclusion**
 - Suggests that treatment with moderate hypothermia appears to improve outcomes in patients with coma after resuscitation from OHCA



Initial ILCOR Advisory Statement

Recommendations made in October 2002

- Unconscious adult patients with ROSC after OHCA should be cooled to 32 – 34 °C for 12 to 24 hours when the initial rhythm is VF
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest

Nolan, et al. (2003). *Circulation*.

Inclusion/Exclusion Criteria

- Early studies conducted with VF & Pulseless VT patients only
- Oddo et al (2008) concluded that time from collapse to ROSC strongly associated with outcomes.

“Only 3.1% of patients with time to ROSC > 25 minutes survived, as compared to 65.7% with time to ROSC ≤ 25 minutes” (p. 2296)

2015 ILCOR/AHA Recommendations

- TTM is recommended for “comatose (ie, lack of meaningful response to verbal command) adult patients with ROSC after cardiac arrest.”
- Shockable & non-shockable rhythms
- OHCA & in-hospital arrests
- Maintain a temperature between 32°C & 36°C
- Cool for at least 24 hours
- **Not** to initiate PRE-hospital cooling by EMS

Callaway et al. (2015). p. S467-8

TTM Trial

“Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest”

Conclusion:

- In unconscious survivors of out-of-hospital cardiac arrest of presumed cardiac cause, hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C.

Nielson, N. et al. (2013). *N Engl J Med* 2013;369:2197-206.

So what does this mean for TH?

- **TTM Trial**
 - Did not include Asystole patients; included VT/VF and PEA, witnessed with immediate CPR (74%)
 - Suggests that for all patients with ROSC, even if not doing TH, aggressive temperature control to prevent hyperthermia is beneficial.
- **Proposed**
 - Consider using 36 degrees if patient hemodynamically unstable at 34 degrees (16 of the 20 patients required vasopressor support at some point). Could be from myocardial stunning, which is not uncommon. Not currently trending when the patient is put on the vasopressor or how long it is on.
 - Aggressively manage hyperthermia in all CA patients regardless of initial rhythm and TH.



Important Information to Obtain

- Witnessed or unwitnessed?
- How long down before CPR initiated?
- Initial rhythm?
- Defibrillated? How many times?
- Time of ROSC?
- Total time from collapse to ROSC?

More Important Information

- Advanced Directive?
- Allow natural death? DNR?
- Dementia?
- Emesis during intubation?
- LOC after ROSC?
- Pre-hospital 12-Lead ECG?
 - ST segment ↑
 - QT prolongation?
- Medications given in the field?
 - Sedation?
 - Paralytic?
 - Amiodarone?



Relative Inclusion Criteria

- VT/VF cardiopulmonary resuscitation, PEA post-cardiac arrest with ROSC & persistent coma as evidenced by not following verbal commands
- Estimated interval of **10 minutes** or less from patient collapse to first resuscitation attempt
- An interval of \leq equal to 25 minutes (PEA) or 60 minutes (VF/pulseless VT) from collapse to ROSC
- Age 18 years or older
- Time of initiation of hypothermia < 6 hours ROSC
- MAP >60 mmHg either spontaneously or with fluids & vasopressor

Conditions to Consider Prior to TTM

- Comatose state prior to arrest
- Pre-existing DNR status
- Metastatic cancer or other terminal illness
- Active sepsis
- Active severe bleeding
- Platelet count < 50 K
- Non-intubated patient
- Cerebral Performance Category of 3 or 4

Outcomes:

Cerebral Performance Categories (CPC)

- **CPC 1: Full Recovery**
 - conscious and alert, able to work and to lead a normal life
- **CPC 2: Moderate disability**
 - conscious, able to work at least part time, and independent for their ADL, with or without neurologic manifestations such as hemiplegia, seizures, ataxia, dysarthria, dysphagia, or permanent memory or mental changes

Wolfrum et al. (2008). *Critical Care Medicine*, 36(6), p. 1783

Outcomes:

Cerebral Performance Categories (CPC)

- **CPC 3: Severe disability**
 - conscious, but fully dependent on others for daily support because of severely impaired cognitive function; these patients are discharged to institutions or long-term rehabilitation facilities
- **CPC 4: Persistent vegetative state**
- **CPC 5: Death**

Wolfrum et al. (2008). *Critical Care Medicine*, 36(6), p. 1783

Cooling the Patient

- Cooling Adjunct Therapies
- Surface Cooling
- Endovascular Cooling



Deye et al. (2015)

Time to Target Temperature

- Studies show time to target temperature to be an independent predictor for good outcome.
- Patients with good outcomes demonstrated a greater drop in T after 1 hour & reached target temp faster (Wolff et al, 2008)



Sendelbacha, S. et al. (2012). *Resuscitation*

Induction of TH

- Initial temperature & temperature monitoring
- Chilled Normal Saline (NS)
 - Supported by many studies: Bernard (2008); Kim et al (2007); Larsson & Rubertsson (2010)
 - 30-40ml/kg, up to 2 liters, of 4°C NS
 - Infuse over 30-60 minutes
 - Decreases core temperature by 1.6-2°C
- Ice Packs



Induction Phase

- Controlling shivering
 - Most likely to occur when core Temp. 34-36°C
 - Wrap hands/feet in warm blanket; Bair hugger
 - Medications: Meperidine? Propofol?
 - Neuromuscular Blocking Agents (NMBA)
 - Before cooling
 - During cooling
 - During rewarming
 - EEG monitoring



Induction Phase

- Sedation
 - Initiate prior to giving a paralytic
 - Fentanyl bolus/infusion
 - Midazolam bolus/infusion



Case 1: Mrs. D



- Mrs. D collapsed at church. She was removed to the foyer where CPR was performed by an EMS-trained bystander.
- Although an AED was present on-site, it was not used.
- EMS arrived within 4-5 minutes. She received a total of 2 shocks for v.fib by FD EMS. She experienced ROSC. Cardiac monitor showed SR after 2nd shock.
- Patient presents unconscious to the ED s/p resuscitation of a v.fib cardiac arrest.



Life-saving treatments for SCA

- **Automatic External Defibrillators (AEDs)** can increase the survival rate for SCA up to 90% by delivering a life-saving shock within the first few minutes of an attack, but they are still not widely available and people often do not know how to use them.
- **Implantable Cardioverter Defibrillators (ICDs)** are 98% effective at protecting those at risk for SCA, but only 35% of patients who could be helped by one, have them.

Source: <http://www.stopcardiacarrest.org/about-sudden-cardiac-arrest/general-information.aspx>

Case 1: Mrs. D.

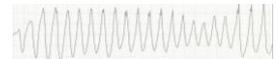
- In the ED:
 - “Code Ice” called
 - VS: T 96.2°
 - Ice packs placed
 - Chilled NS infusion initiated
 - King LT replaced with ETT
 - Central line placed
 - OG & foley placed
 - Labs sent
 - AMI work up done: ECG (QTc 503ms); enzymes
 - Consults to neurology & pulmonology
 - Propofol initiated
 - Repeat T after NS: 93.1°

Case 1: Mrs. D

- Transferred to CCU
- Surface cooling with sleeves initiated
- Frequent VS monitoring
- SB, no ectopy
- Re-warmed without complications
- EF 55-60% the day after CA
- Cardiac cath: no significant disease
 - 2/3 of SCA deaths occur in people without any prior indications of heart disease
- ICD placed to prevent recurrence of sudden death
- Discharged 13 days after CA with CPC 1

Case 2

- 30 yo female, 2 weeks post-partum
- 12/22 Went to Patient First with chest pains
- Had a seizure at Patient First; MD administered 2 mg Ativan
- Patient went into cardiac arrest 1 min. later
- CPR; EMS called 2144; EMS arrived 2154
- Polymorphic VT initial rhythm
- Defibrillated 200 joules



EMS

- What are your next steps?



Case 2, cont

- 2220 Patient unresponsive post-ROSC; GCS 3
- 2220 On the way to the hospital, RSI performed to protect the patient's airway
- Medications administered
 - 2220 Magnesium 2 mg
 - 2230 RSI: Vecuronium 7 mg; Versed 3 mg

What next?



Case 2, cont

- 2237 In ED, patient unresponsive
- CT done
- Code Ice called
- Ice packs applied
- Total of 2 L chilled NS administered
- K+ 2.5 on admission
- Initial T 97.7 °
- Endovenous catheter inserted
- Consults
 - Cardiology
 - Pulmonology
 - Neurology

Case 2, cont.

- 12/23, 0017 to CCU
 - 0200 95.9 °
 - 0300 93 °
- Cooled for 24 hours

Maintenance Phase

- Monitoring for complications
- “Cold” diuresis
- Electrolyte shifts
 - Potassium
 - Magnesium
 - Ionized calcium
 - Phosphorous
- Cardiac Dysrhythmias



Maintenance Phase

- Insulin Resistance & Hyperglycemia
 - Survival to discharge higher in non-diabetic patients
 - Target moderate glycemic control: 144 to 180 mg/dL
 - Avoid hypoglycemia

Beiser, et al. (2009). *Resuscitation*

Maintenance Phase

- Other complications to monitor for during TH
 - Bleeding: impaired platelet aggregation; ↑ clotting times
 - Infection: Pneumonia
 - Skin breakdown if surface cooling
 - ↓ metabolism
 - CV: VT/VF; atrial fibrillation; Prolonged PR, QRS, QTc; sinus bradycardia

Re-Warming Phase

- Passive versus active re-warming
- If active, very slow process to avoid rebound hyperthermia
- Risk of hyperkalemia
- Shivering



Prognostication in TH Patients

- TH has improved outcomes in 1 of 6 patients
- No studies exist that detail the prognostic accuracy of the neurological examination in TH patients
- Multimodality assessment needed.
- Early withdrawal of life support may not be in the best interests of TH patients & families.

Neumar, et al. (2008). *Circulation*
 Peberdy et al. (2010). *Circulation*
 Rossetti, A.O.; Rabinstein, A.A. & Oddo, M. (2016). *The Lancet/Neurology*

Case 2, cont.

- Re-warmed
- Extubated 12/24
- Transferred to floor 12/26
- Discharged to home 12/30
- Returned in January for Cardiac Cath & EP studies
 - EF 40%
 - EP study negative

Case 3

- 54 yo female c/o SOB
- EMS called
- After EMS arrival, patient becomes unresponsive. No pulse.
- What do you do?

Case 3, cont.

General CA management

- CPR
- Assess rhythm



- Administer Medications
 - Epi 1 mg
 - 4 doses given
- ROSC
- Approximately 8 min downtime
- Start chilled NS
- Protect airway
- Avoid hyperoxygenating
- Transport

Case 3, cont.

- In ED, unresponsive
- Code Ice Initiated
- BP dropped, MAP < 60
 - Chilled NS infusing
 - Norepinephrine started
- Bradycardia → PEA
 - CPR
 - Epi
 - Atropine
 - ROSC within 5 min
- Intubated
- SpO2 60-70's despite interventions
- Chest X-ray showed pulmonary edema—Lasix administered
- BP MAP < 60
 - Phenylephrine started
- Unable to maintain MAP > 60; hypoxia persisted

Case 4

59 yo male out in yard spraying a wasp nest.
 Reports being stung to family when goes in house. C/o SOB and "not feeling well."
 Patient lies down on bed. Stops breathing.
 Family immediately calls 9-1-1 and begins CPR.
 EMS responds within 11 minutes. EMS read the ECG as "vfib" and shocked the patient x2

Case 4, cont.

- Cont. CPR
- Insert IV
- Administers epi 1mg x2 & amiodarone 300mg; Amiodarone 150mg over 10 min
- ROSC
- EMS inserts King LT
- Transports to ED, 7/18 at 1323
- Patient unconscious

Case 4, cont. In ED

- PMH: HTN; hyperlipidemia
- Positive for ETOH (12 beers/day) & 3 pack per day smoker
- Drug screen positive for ETOH & benzos
- ED physician has difficulty placing ETT secondary to angioedema
 - Patient bradycardic → PEA
 - Brief round CPR & Atropine 1mg
 - ROSC

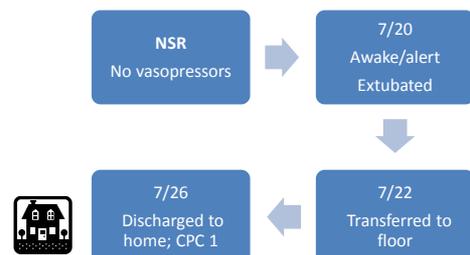
Case 4, cont. in ED

- Received treatment for anaphylaxis & angioedema
 - Benadryl
 - Subcut. Epi
 - Solumedrol
 - Large volumes of chilled NS (2 Liters)
- Endovenous cooling catheter placed
- Echo showed normal function (EF 60%)
- Transported to CCU

Case 4, cont. In CCU

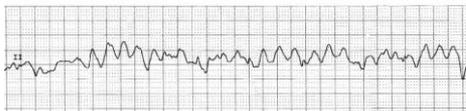
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|---|--|
| <ul style="list-style-type: none"> • Notable admission labs <ul style="list-style-type: none"> – WBC 18 – Hgb 17.7 – ABGs <ul style="list-style-type: none"> • Ph 7.03 • PaO2 428 • Bicarb 14.3 • BE -16.9 – K⁺ 3 | <ul style="list-style-type: none"> • Treatment <ul style="list-style-type: none"> – Pan-cultured – Antibiotics – Electrolyte replacement – Fluid resuscitation – Bicarb drip – Pepcid – "Goody bag" – Sedation |
|---|--|

Case 4, cont. in CCU



Case 5

- 26 y.o. female OHCA. Pt found responsive on the floor by husband. Pale and gurgling.
- 911 called; operator instructed CPR performed by husband until EMS arrival
 - Initial rhythm



Case 5, cont.

- Defibrillated with ROSC
- CM: Tachycardia
- PMH: Crohn's disease; HTN treated with weight reduction; smoker
- Recent history: acute bronchitis; RUQ pain; c/o dizziness at work & with exercise; never passed out

Case 5, cont.

- To ED, initiated Code Ice (10/02)
- Chilled NS
- King LT (+ emesis during CA) → Intubated
- 1454 HR 153; Metoprolol given
- 1530 Patient to card cath lab (EF 60%)
- K⁺ 2.9 Gluc 243 BUN 4 Cr 0.7
- WBC 24

Special Considerations



- If the patient is also an AMI, follow AMI protocols
- Cooling will still be initiated even if going to cath lab—start chilled saline & apply ice packs
- Do not delay transport to cath lab for endovenous catheter insertion—can be done after the cardiac catheterization

Case 5, cont.

- Cooled for 24 hours
 - Fentanyl
 - Midazolam
 - Phenylephrine to keep MAP > 60 mmHg
 - Hypoglycemia → D10
- Extubated 10/04
- 10/10: ICD implanted 2° prolonged QT
- 10/11: Discharged to home; CPC 1

Questions?



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