Therapeutic Hypothermia after Cardiac Arrest

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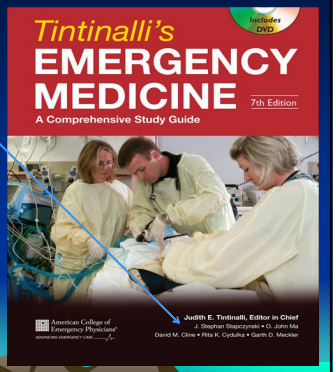


Cardiac Arrest Statistics

- 225,000 out-of-hospital cardiac arrests occur each year in the United States
- Survival to ED admission:
  - Typical: < 10%
  - Seattle: ≈ 50%
- Survival to hospital discharge
  - Typical: < 3-4%
  - Seattle: ≈ 15-20%

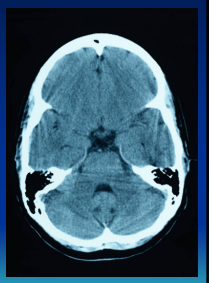
Does Post-Arrest In-Hospital Care Matter?

- Previous studies before 2000 suggested that hospital care did not influence out-of-hospital cardiac arrest patient outcome.
- Not true anymore
- Hospitals can give treatment to improve survival

Resuscitation 2003; 56:247

Neurological Death

- 60% of patients admitted to ICU following cardiac arrest die prior to discharge
- A number have permanent disability
- Why? Brain injury



Intensive Care Med 2004;30:2126

What Makes the Difference

- Therapeutic Hypothermia (RCT)
- Percutaneous Coronary Intervention (observational)
- Overall supportive care (observational)

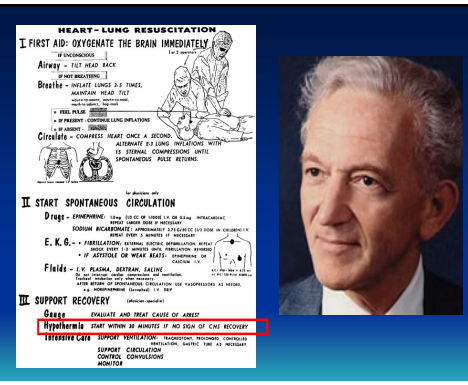
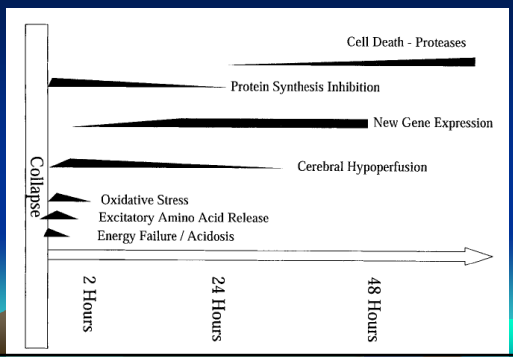


Figure 2. The *first* cardiopulmonary cerebral resuscitation (CPCR) system, composed by Safar in Pittsburgh in 1961. Reproduced from: Safar P. Community-wide CPR. J Iowa Med Soc. 1964: (Nov):629–35. Reprinted with permission of the Iowa Medical Society.

How does cooling work?

Reperfusion Injury



What clinical evidence demonstrates that cooling is effective?

The HACA Trial

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*

- Multicenter: 9 hospitals, 7 cities, 5 countries throughout Europe

Protocol

- Witnessed cardiac arrest
- Initial rhythm VF or non-perfusing VT
- 5 to 15 min emergency personal response
- ROSC within 60 min
- Block randomization in groups of 10, stratified according to center
- External cooling
- Target temperature 32-34 °C for 24 hours after cooling started
- Passive rewarming
- 3551 evaluated and 275 enrolled in study

HACA Results

- "Favorable" neurological outcome at 6 months
  - 75/136 (hypothermia) versus 54/137 (controls)
  - 55% (hypothermia) versus 39% (controls)
- Deaths by 6 months
  - 41% (hypothermia) vs. 55% (controls)
- Non-significant trend to more complications in 1st week in the hypothermia group
  - 22% more complications, including: pneumonia, bleeding & sepsis

HACA: Survival Curve

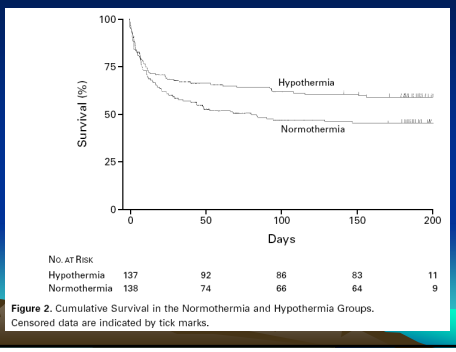


Figure 2. Cumulative Survival in the Normothermia and Hypothermia Groups. Censored data are indicated by tick marks.

Melbourne, Australia

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. Buist, M.B., B.S., Bruce M. Jones, M.B., B.S., William Silvester, M.B., B.S., Geoff Gutteridge, M.B., B.S., and Karen Smith, B.Sc.

Four participating EDs/Hoitals

Protocol

- Initial rhythm VF
- Successful ROSC
- Persistent coma
- Transfer to one of four participating EDs
- Odd-Even day of the month randomization
- External cooling
- Target temperature 33℃
- Duration was 12 hours after arrival
- Active re-warming at 18 hours
- 84 patients eligible and 77 enrolled in study

Outcome at Hospital D/C

- "Good" outcome = alive with discharge to home or rehab facility
- 49% in hypothermia
- 26% in normothermia controls
- OR = 2.65; 95% CI 1.01 – 6.98

Table 5. Outcome of Patients at Discharge from the Hospital.

Outcome*	Hypothermia (N=43)	Normothermia (N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing facility)	0	1
Severe disability, unconscious (discharged to a long-term nursing facility)	0	1
Death	22	23

*The difference between the rates of a good outcome (normal or with minimal or moderate disability) in the hypothermia and the normothermia groups (49 percent and 26 percent, respectively) was 23 percentage points (95 percent confidence interval, 13 to 43 percentage points; P=0.046). The unadjusted odds ratio for a good outcome in the hypothermia group as compared with the normothermia group was 2.65 (95 percent confidence interval, 1.02 to 6.88; P=0.046). The odds ratio for a good outcome in the hypothermia group as compared with the normothermia group, after adjustment by logistic regression for age and time from collapse to return of spontaneous circulation, was 5.25 (95 percent confidence interval, 1.47 to 18.76; P=0.011).

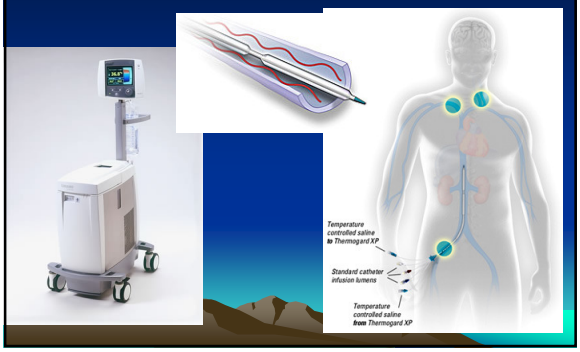
Favorable or Good Outcome

- HACA Study
  - 75/136 (55%) versus 54/137 (39%)
  - Absolute difference =16% (95% CI 4-27%)
  - NNT ≈ 8
- Melbourne Study
  - 21/43 (49%) versus 9/34 (26%)
  - Absolute difference = 22% (95% CI 1-43%)
  - NNT ≈ 5

How are patients cooled?

Surface Cooling

Internal Cooling

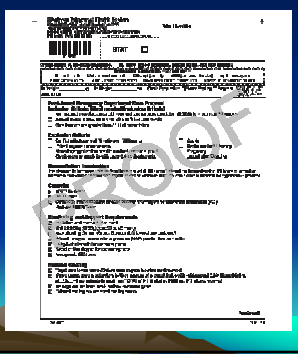


Multidisciplinary Approach Necessary

- Emergency Medicine
- Cardiology
- Cardiothoracic surgery
- Neurology
- Critical care physicians
- ICU nursing

Predefined Protocol Essential

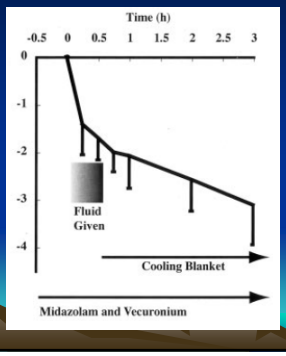
- Sedation
- Muscular paralysis
- Internal temperature monitor
- Avoid overshoot



Clinical Approach

- Can initiate with ice-cold NS and external ice bag cooling
- Target temperature is 32-34°C
- Likely to achieve target temperature fast
- Initiate as quickly as possible – ideally in the ED
- Can continue while in cath lab and then ICU

Cooling Strategy



Cold IV Fluids

- 19 clinical studies – 6 in prehospital
- No increased incidence of pulmonary edema
- Ice cold (4℃) NS or RL mL/kg (2100 mL in 70 kg adult) over 30 min
- Core temperature typically decreases 1.4 to 1.5℃

Clinical Issues

- Sedation
  - Cooling is uncomfortable
  - Shivering is bad – generates heat
  - Plan to sedate patients according to ICU sedation protocol: midazolam or propofol
- Pharmacological paralysis
  - Needed in most cases during induction of cooling: vecuronium or rocuronium
  - Can be stopped once target temperature achieved
  - Many centers now only resuming paralysis when shivering occurs

Complications

- Bradycardia
  - Often have heart rate below 50.
  - May have heart rate below 40. Watch urine output. If low, then perfusion may be inadequate; and heart rate support could be considered (dobutamine?).
- Hypokalemia
  - When cooled, potassium shifts into cells.
  - Replace K+ to keep level normal ~ 4 mEq/L

Complications

- Excessive cooling
  - Easy to get patient too cold
  - Increases risk of bleeding and infection
  - No additional brain benefit
- More automated cooling devices make excessive cooling less likely

Complications

- Seizures
  - Injured brain at higher risk of seizures
  - EEG monitoring might be useful

2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science – Advanced Life Support

- Comatose adult patients (not responding in a meaningful way to verbal commands) with spontaneous circulation after out-of-hospital VF cardiac arrest should be cooled to 32 to 34°C for 12 to 24 hours..
- Induced hypothermia might also benefit comatose adult patients with spontaneous circulation after out-of-hospital cardiac arrest from a nonshockable rhythm, or cardiac arrest in hospital.

Circulation 2010;122:S345

2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science – Advanced Life Support

- Rapid infusion of ice-cold IV fluid 30 mL/kg or ice packs are feasible, safe, and simple methods for initially lowering core temperature up to 1.5°C
- Limited available evidence suggests that PCI during therapeutic hypothermia is feasible and safe and may be associated with improved outcome.

Circulation 2010;122:S345

2010 AHA Guideline Post-Cardiac Arrest Care

- Comatose (ie, lack of meaningful response to verbal commands) adult patients with ROSC after out-of-hospital VF cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours (Class I, LOE B).
- Induced hypothermia also may be considered for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIb, LOE B).

Circulation 2010;122;S768

2010 AHA Guideline Post-Cardiac Arrest Care

- 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).

Circulation 2010;122;S768

Who Not to Cool

- Cardiac arrest after hanging
  - Case reports only
  - One retrospective observational study of 13 patients comatose after hanging but only 3 had sustained cardiac arrest
  - No controlled clinical trials
- Cardiac arrest after submersion ("near-drowning")
  - Mixed bag of case reports
  - Often complicated by cold water submersion with accidental hypothermia

Who Not to Cool

- Traumatic cardiac arrest
  - No clinical studies
  - Mixed bag of patients – blunt versus penetrating, many with associated neurotrauma, some undergoing surgery
  - Nightmare of the surgeon – increased risk of bleeding

Rewarming

- Stop potassium infusion (if present)
- Set cooling device to slowly rewarm patient to 36℃ over 6-10 hours
- May need to reinstitute paralytic if shivering becomes a problem.
- Discontinue paralytic at 35℃ and discontinue sedation at 36℃.

Summary

- Evidence supports use of therapeutic hypothermia for comatose survivors of out-of-hospital cardiac arrest
- Should be initiated ASAP after ROSC, but appears successful even if delayed (e.g. 4-6 hours).
- Target core temperature should be to 32-34℃ for 12-24 hours
- Slow rewarming over ≥ 6 hours.

The two major questions

- Can we do it? YES
- Should we do it? YES

- **Teşekkür ederim!**