Targeted Temperature Management

Understanding the Evidence

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Sound Critical Care

AdventHealth Tampa

Why Does TTM Matter to a Hospitalist?

- A hospitalist is an inpatient medicine specialist
- Targeted temperature management/TTM is a shared decision
- TTM is a challenging decision based on available evidence
- Many hospitalists provide care to patients in intensive care units
- Cardiac arrests (out-of-hospital or inpatient) don’t discriminate between community hospitals and academic medical centers

Learning Objectives

- Understand evidence motivating targeted temperature management/TTM
- Contemplate indications and relative contraindications to TTM
- Review strategies for initiation of TTM and management of complications associated with TTM

Jane Doe

- Middle-aged female
- Found down in a hotel room by maid two hours after check-out time
- No emergency contact, surrogate decision maker or witness
- No known past medical history
- No known medications

- EMS found patient with agonal respirations and no pulse
- Monitor: Ventricular fibrillation
- ACLS initiated by EMS
- Epinephrine x6, defibrillation x3, amiodarone 300mg x1, amiodarone 150mg x1, lidocaine 100mg x1, calcium chloride 1000mg x1, CPR, LMA insertion
- ROSC achieved on arrival to ED

Jane Doe

T: 32.3C

HR: 152/min

BP: 74/39mmHg

SpO2: 82% on FiO2 100%

Not sedated, unresponsive, GCS5T

Pupils minimally reactive, absent corneal reflex B/L

Absent cough reflex, absent gag reflex

Tachycardic, no murmur

Decreased breath sounds at R hemithorax, no wheezes, no crackles, subcutaneous emphysema

Soft abdomen, non-distended abdomen

Does not follow commands

Minimal withdrawal to noxious stimuli at UE B/L

Minimal withdrawal to noxious stimuli at LE B/L

- Initial laboratories

WBC 29.4 with 22bands

Hgb 12.9

Platelets 149

INR 2.21

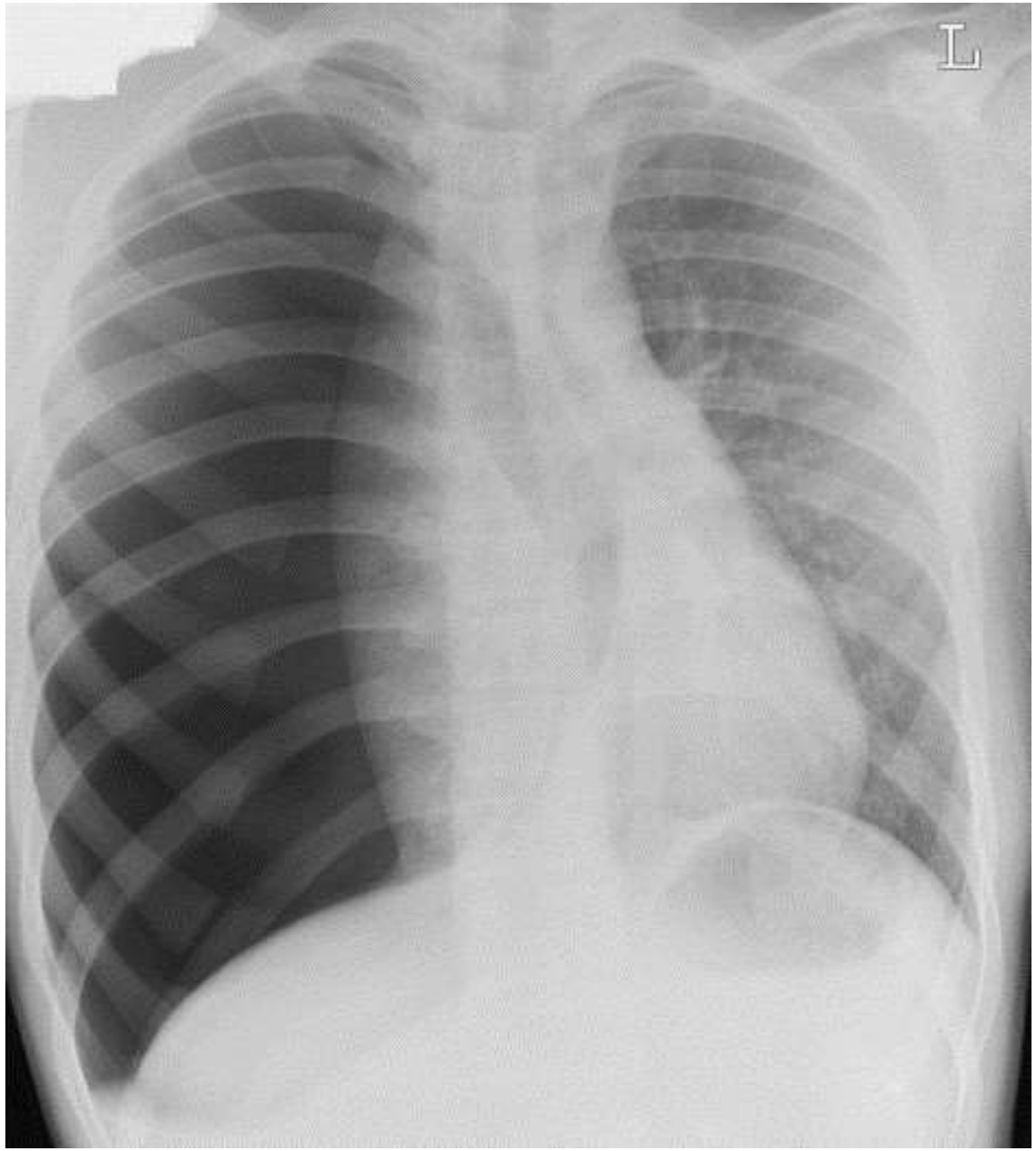
BUN 25

Creatinine 2.1

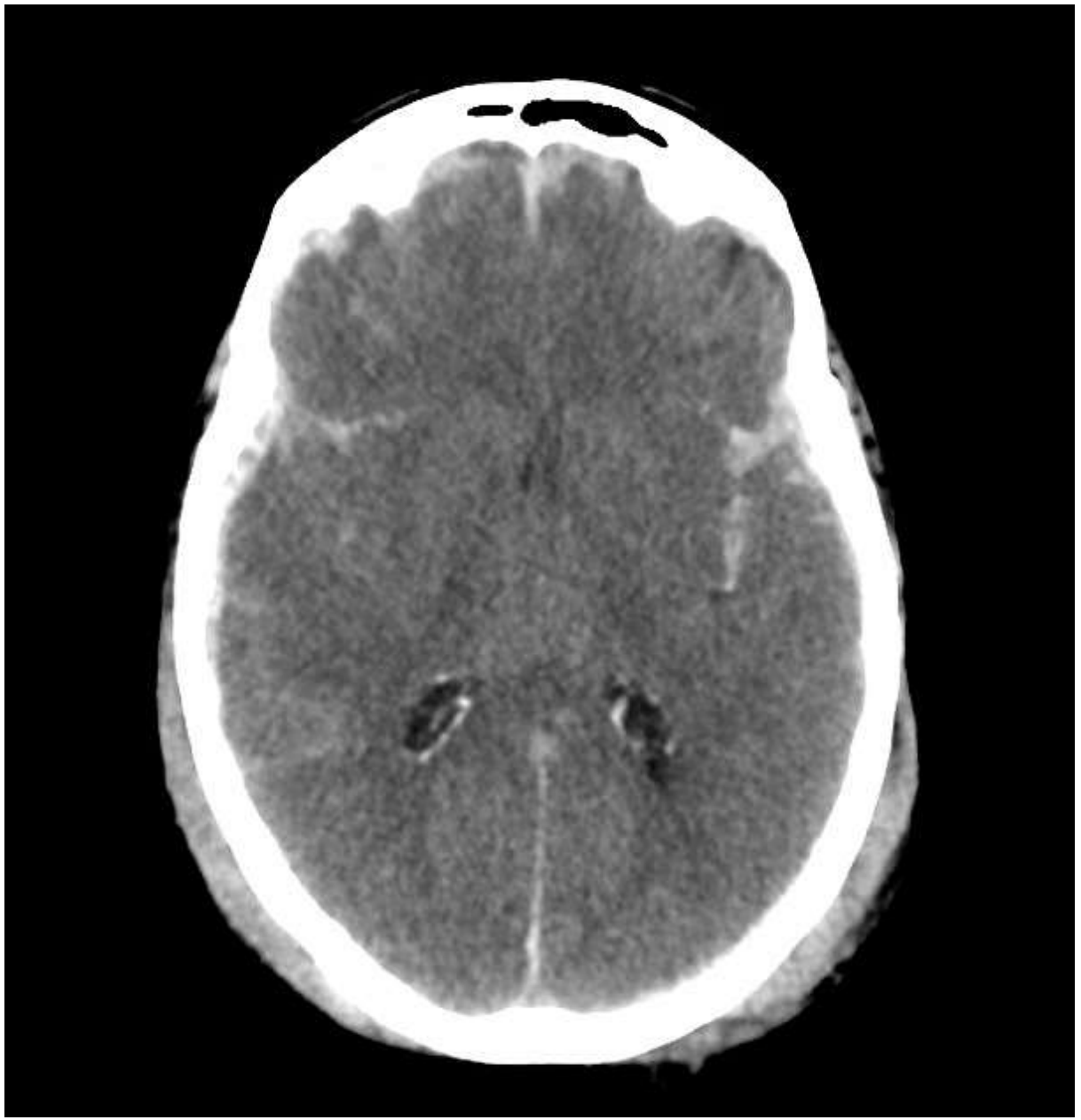
Potassium 5.9

Lactic acid 17.1

ABG: 6.81/102/64 on FiO2 100%



https://www.resuscitationjournal.com/article/S0300-9572(05)00421-1/fulltext



https://radiopaedia.org/cases/diffuse-cerebral-oedema

Considerations?

- RIGHT NOW

How do I keep her alive?
Where's my chest tube?
Where's my vasopressor?
What's my central access?
Is she getting fluids?
Is she getting antibiotics?
Needs more imaging?

- SOON

Surrogate decision maker?
Medical history?
Etiology to arrest?
Cardiology consult?
Cardiac catheterization?
Diffuse cerebral edema?

Targeted temperature management?
Referral to OPO?
Start? Stop?

Why Should We Care?

- Cardiac arrest is common!
  - OOHCA >600,000/year worldwide
  - IHCA >290,000/year worldwide
- Survival after cardiac arrest could be better!
  - OOHCA: 10% survival
  - IHCA: 30% survival
- Functional recovery after cardiac arrest remains a priority!
  - Potential role for targeted temperature management
- Down time is functional loss time!
  - Free radical generation occurs after five minutes of cardiac arrest

- Could the next cardiac arrest patient be you?
- Could the next cardiac arrest patient be someone you know or love?

Foundations for Targeted Temperature Management

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Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Review

Targeted temperature management after cardiac arrest. A systematic review and meta-analysis of animal studies

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Foundations for Targeted Temperature Management

TABLE 2. NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02

*The risk ratio was calculated as the rate of a favorable neurologic outcome or the rate of death in the hypothermia group divided by the rate in the normothermia group. CI denotes confidence interval.

†Two-sided P values are based on Pearson's chi-square tests.

‡A favorable neurologic outcome was defined as a cerebral-performance category of 1 (good recovery) or 2 (moderate disability). One patient in the normothermia group and one in the hypothermia group were lost to neurologic follow-up.

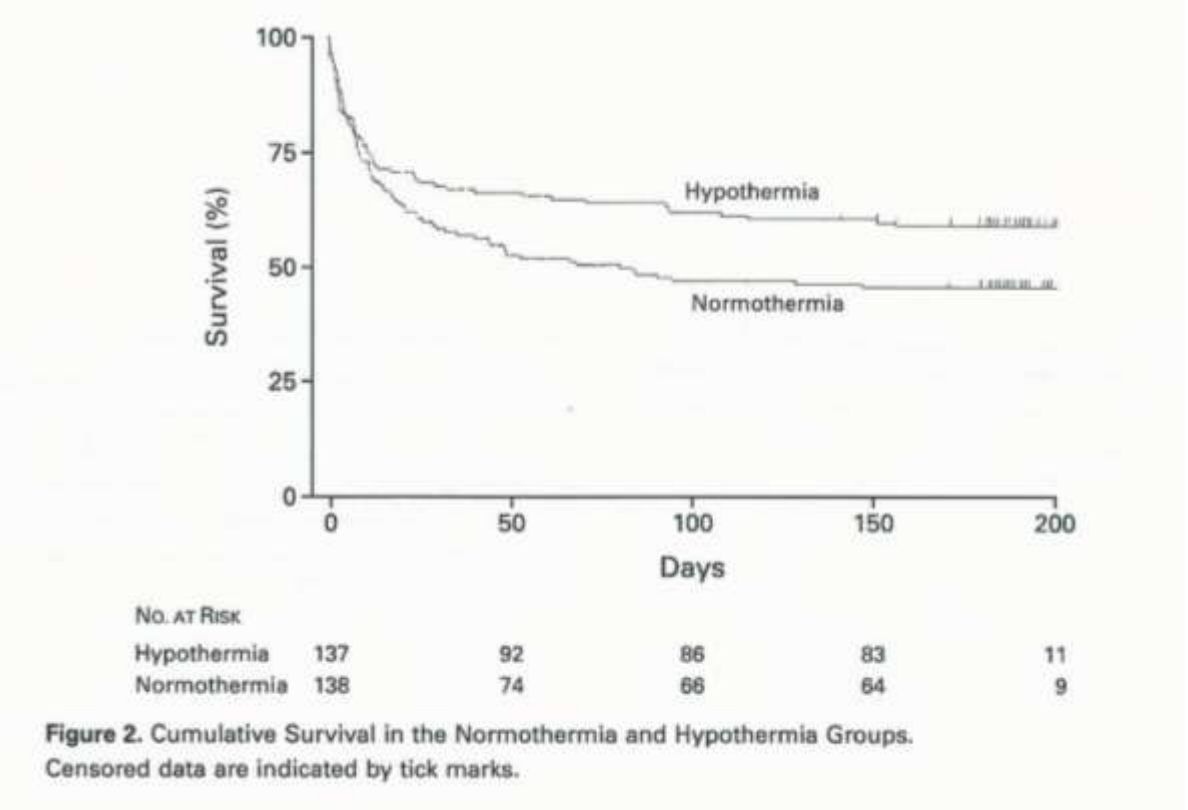


Figure 2. Cumulative Survival in the Normothermia and Hypothermia Groups. Censored data are indicated by tick marks.

Hypothermia After Cardiac Arrest Study Group. "Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest." *NEJM*. 346(8): 549-556. 2002.

Selecting a Patient for TTM

Indications

- Shockable OOHCA
- Other cardiac arrests

+

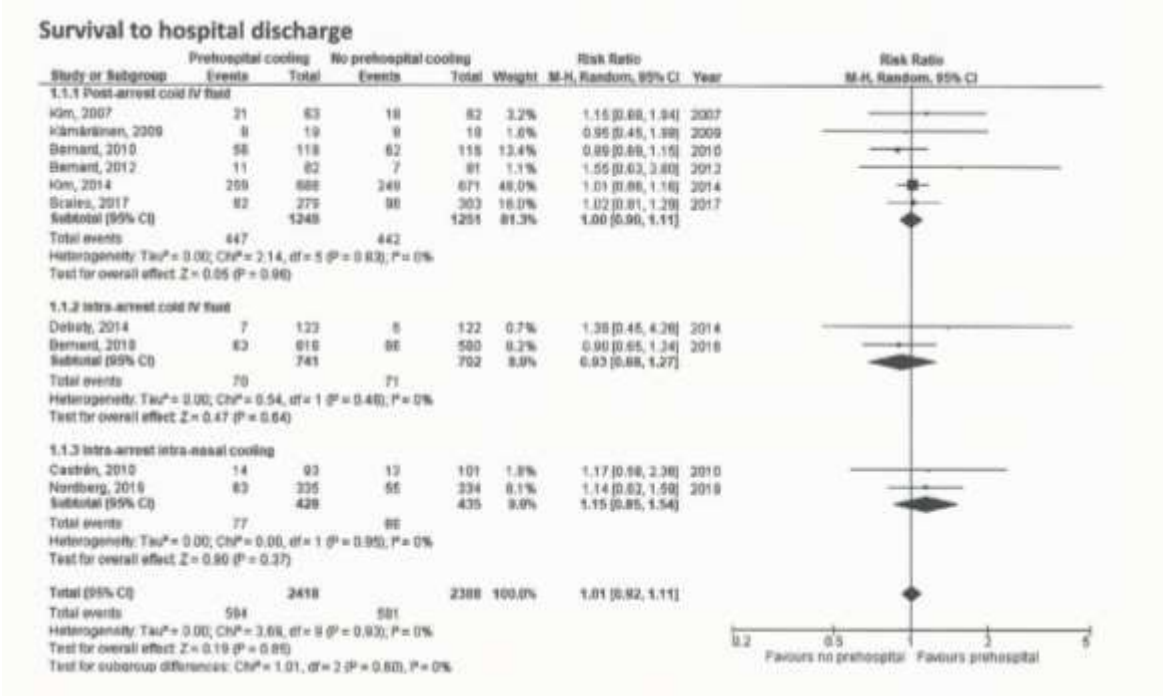
- Neurologic injury

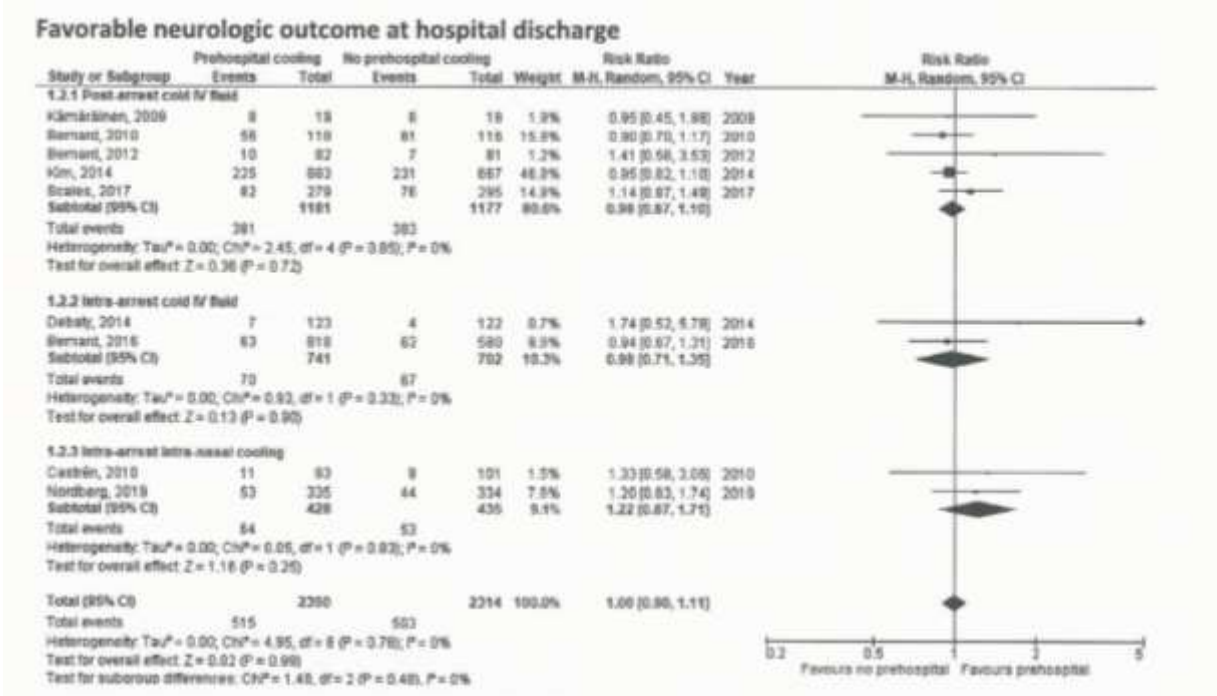
Contraindications

- No anticipation for meaningful neurologic recovery
- >12hours since arrest

- ?Intracranial hemorrhage
- ?Bleeding diathesis

Pre-hospital Cooling





Granfeldt, A., et al. “Targeted temperature management in adult cardiac arrest: Systematic review and meta-analysis.” *Resuscitation*. 167: 160-172. 2021.

Selecting a Temperature for TTM

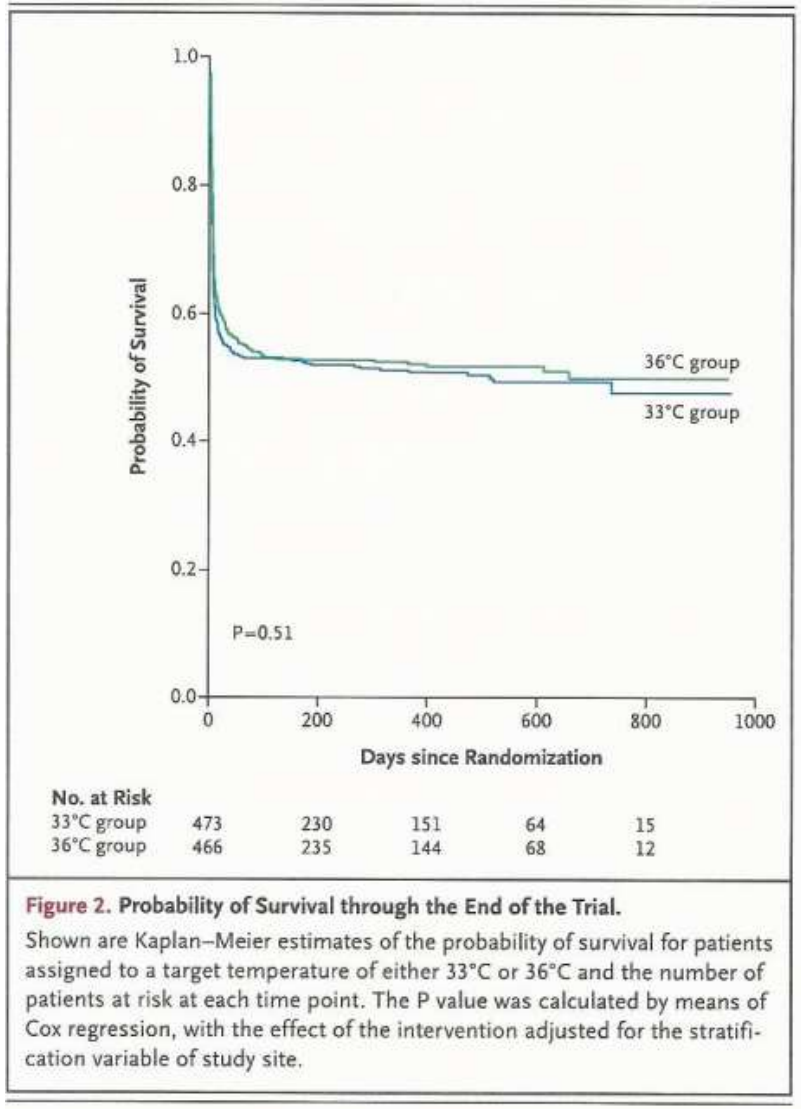


Figure 2. Probability of Survival through the End of the Trial.
Shown are Kaplan–Meier estimates of the probability of survival for patients assigned to a target temperature of either 33°C or 36°C and the number of patients at risk at each time point. The P value was calculated by means of Cox regression, with the effect of the intervention adjusted for the stratification variable of study site.

Nielsen, N., et al. "Targeted Temperature Management at 33'C versus 36'C after Cardiac Arrest." *NEJM*. 369(23): 2197-2206. 2013.

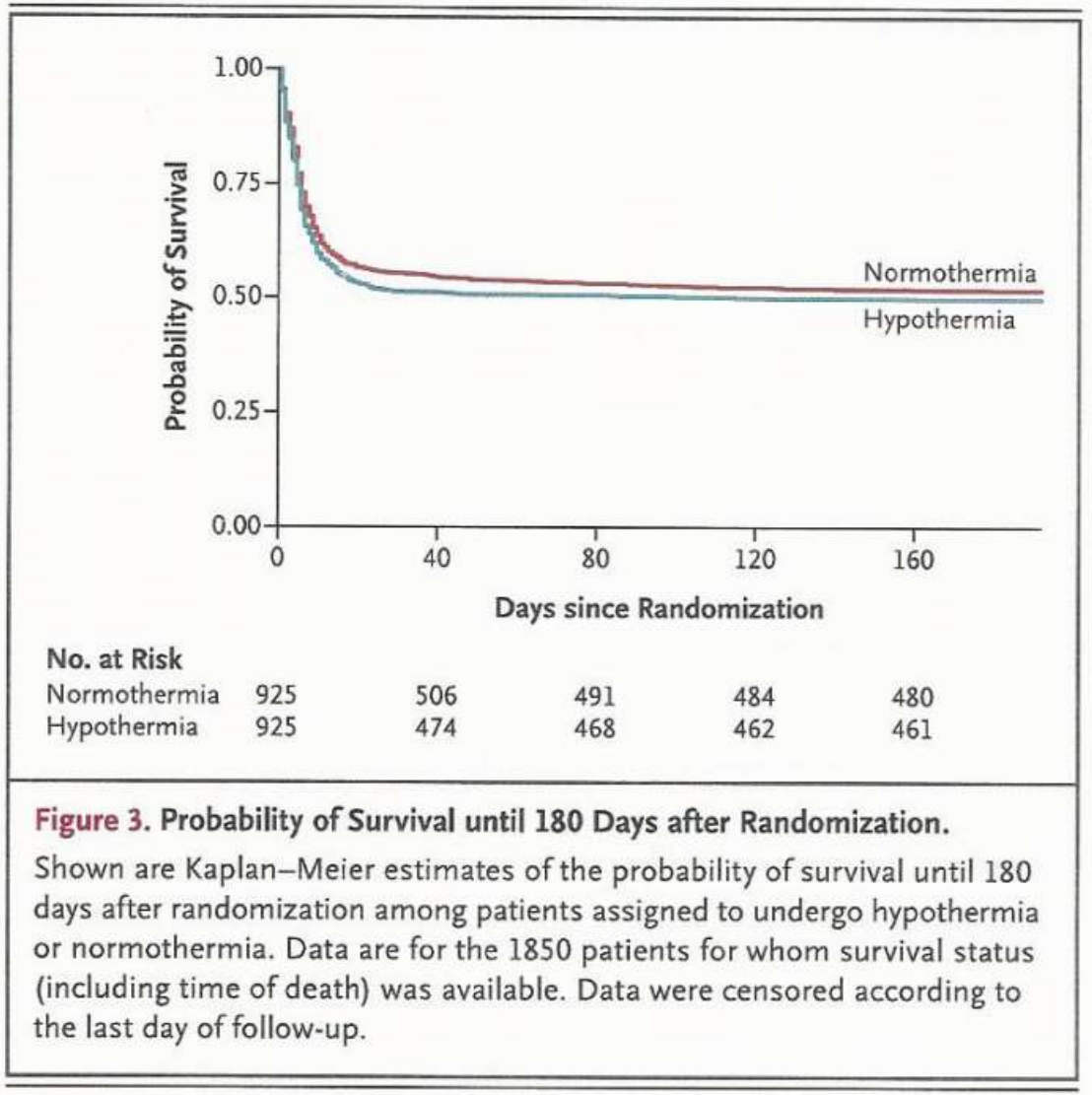


Figure 3. Probability of Survival until 180 Days after Randomization.
Shown are Kaplan–Meier estimates of the probability of survival until 180 days after randomization among patients assigned to undergo hypothermia or normothermia. Data are for the 1850 patients for whom survival status (including time of death) was available. Data were censored according to the last day of follow-up.

Dankiewicz, J., et al. "Hypothermia versus Normothermia after Out-of-hospital Cardiac Arrest." *NEJM*. 384(24): 2283-2294. 2021.

Implementing TTM

- Esophageal probe temperature
- Goal time for initiation of TTM

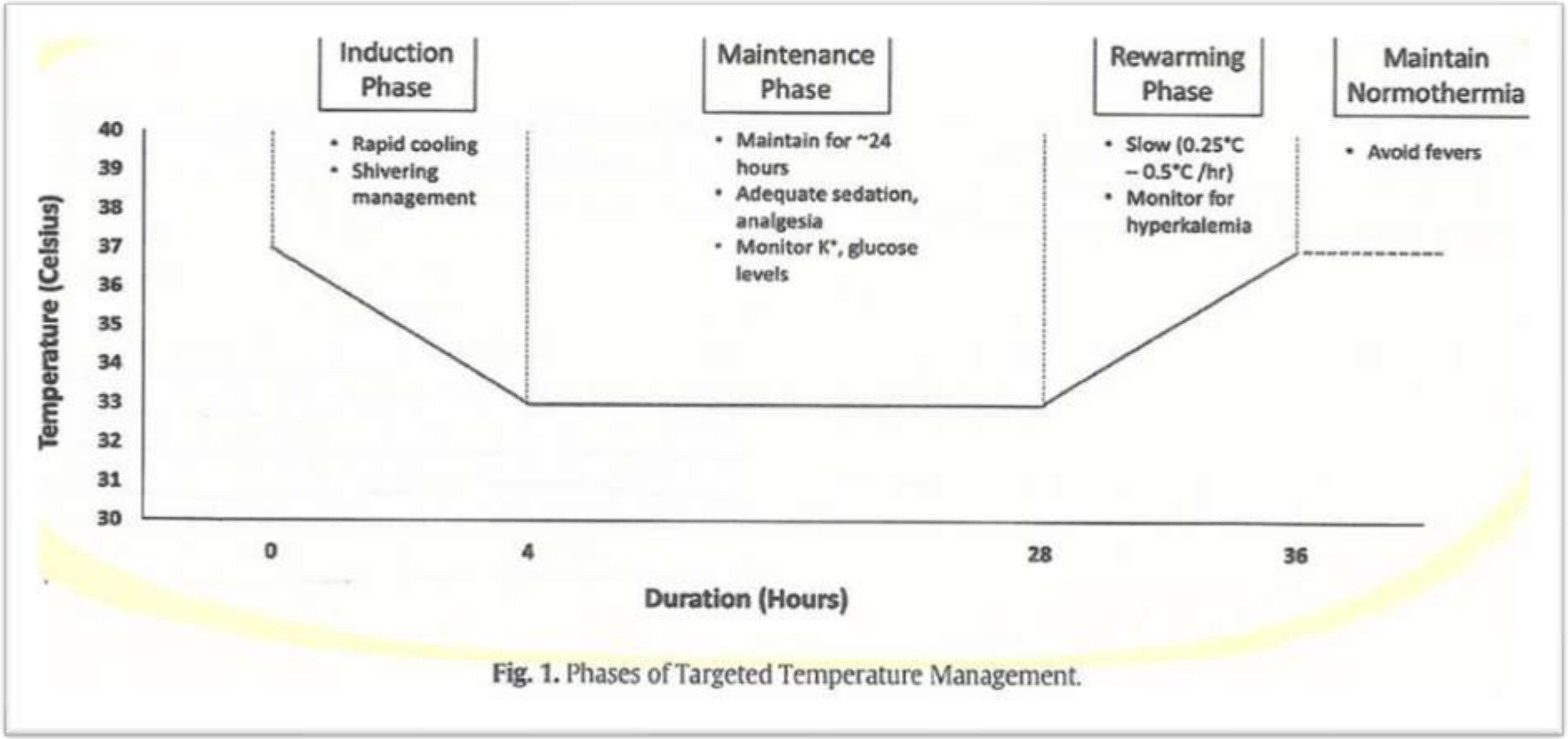


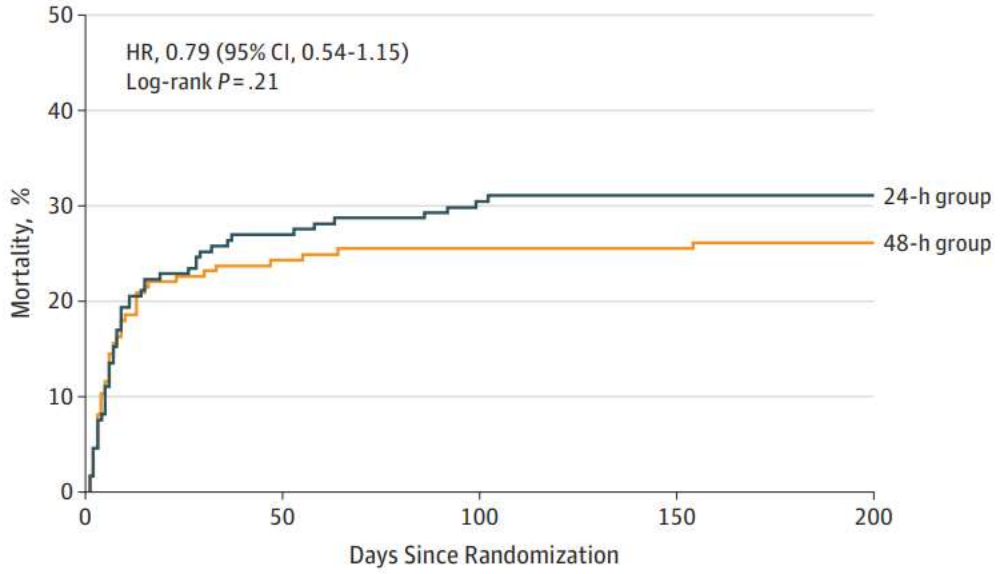
Fig. 1. Phases of Targeted Temperature Management.

Mody, P., et al. "Targeted temperature management for cardiac arrest." *Progress in Cardiovascular Diseases*. 62: 272-278. 2019.

Duration of TTM

24HR v. 48HR v. 72HR v. LONGER

Figure 3. Probability of Death With Standard and Prolonged Targeted Temperature Management.



Kaplan-Meier probability of death from randomization to 6 months (200 days) in the study groups. Median follow-up time was 184 days (IQR, 33-196 days) in the 48-hour group and 181 days (IQR, 15-193 days) in the 24-hour group.

Kirkegaard, H., et al. "Targeted temperature management for 48 v 24 Hours and Neurologic Outcome after Out-of-hospital Cardiac Arrest: A Randomized Clinical Trial." *JAMA*. 318(4): 341-350. 2017.

Shivering

- I was wrong!
- It's not the same as myoclonus!

- Up to 40% patients receiving TTM
- Cerebral Metabolic Stress

Table Bedside Shivering Assessment Scale[a]

Score	Type of shivering	Location
0	None	No shivering is detected on palpation of the masseter, neck, or chest muscles
1	Mild	Shivering localized to the neck and thorax only
2	Moderate	Shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	Severe	Shivering involves gross movements of the trunk and upper and lower extremities

[a] Data from Badjatia et al.[16]

https://pbrainmd.wordpress.com/2015/12/07/the-columbia-anti-shivering-protocol/

TABLE 2. Suggested Antishivering Protocol

When to Initiate	Typical BSAS Score at Initiation	Intervention	Dose	Goal of Intervention
Before starting temperature management, administer all 3 medications in this category.	0	Acetaminophen	650–1000 mg PO/PR/ NGT mg Q 4–6 h	Prevention of shivering
		Buspirone	30 mg PO/PR/NGT Q 8	
		Magnesium sulfate	0.5–1 g/h IV or 4g bolus; goal serum magnesium level of 3–4 mg/dL	
		Skin counterwarming	43°C/MAX Temp	
When shivering is localized to the neck/thorax; may be seen only as an artifact on ECG or felt by palpation	1	Dexmedetomidine or opioid	Dexmedetomidine 0.2–1.5 mcg/kg/h Fentanyl starting dose, 25 mcg/h Meperidine 50–100 mg IM or IV	Mild sedation
When shivering includes intermittent involvement of the upper extremities ± thorax	2	Dexmedetomidine and opioid	As above Consider continuous IV infusion of fentanyl 0.25–2 mcg/kg/h	Moderate sedation
When generalized shivering or sustained upper/lower-extremity shivering is present	3	Propofol	25–75 mcg/kg/min	Deep sedation
When generalized shivering or sustained upper/lower-extremity shivering is present despite use of medications at preceding levels	3	Rocuronium bolus or cisatracurium infusion or vecuronium bolus or pancuronium bolus	0.3–0.9 mg/kg 1–2 mcg/kg/min 0.08 – 0.1 mg/kg IV 0.04 – 0.1 mg/kg IV	Neuromuscular blockade, last resort after inability to control shivering despite all other medications

Note. If shivering worsens, add sequential interventions as appropriate after increasing numerical score of the BSAS, but continue all lower level interventions. Additional medications in the above classes may also be considered, such as ondansetron, tramadol, ketamine, etc.

Jain, A., et al. "Shivering Treatments for Targeted Temperature Management: A Review." *Journal of Neuroscience Nursing*. 50(2): 63-67. 2018.

Metabolic Changes with TTM

- Hypokalemia
- Hyperkalemia
- Insulin resistance
- Coagulopathy

Complications Associated with TTM

- Pneumonia
- Bradyarrhythmia
- Cold diuresis
- Decreased drug metabolism

Timing for Neuroprognostication after TTM

- Brain death
- Non-brain death

- Age
- Sex

- EEG
- MRI brain
- Five half-lives of medications
- Brain death criteria

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Is TTM Worth the Investment?

- $100-160,000/patient
- Increased nursing care
- Increased ICU length of stay
- Resource allocation

Revisiting Jane Doe

- Underwent endotracheal intubation
- Underwent chest tube insertion
- Received 30mL/kg IVF followed by three vasopressor agents (MAP>65mmHg)
- UDS returned positive for opioids, cocaine, THC
- Deemed a poor candidate for TTM secondary to magnitude of neurologic injury without likely recovery of meaningful function status despite TTM
- EEG revealed no evidence of seizure activity (consistent with brain death)
- “You’re not dead until you’re warm and dead.”
- Family located and agreed to DNR/DNI code status pending brain death evaluation
- Declared brain dead within 24hours admission to MICU
- Referred to OPO for organ donation

Closing Considerations

- TTM is NOT for every cardiac arrest patient
- TTM can be harmful despite its attempt to be helpful
- TTM is heavily resource-consumptive without a guaranteed benefit
- TTM is still endorsed by AHA, ENLS

- Avoidance of hypothermia may be a reasonable TTM alternative
- More research is necessary to determine the ideal temperature and duration of therapy for TTM

Question 1

TTM evidence uniformly demonstrates increased benefit in neurologic outcomes among patients cooled to 32C relative to patients cooled to 36C?

A. True
B. False

Question 2

Which electrolyte abnormality is commonly manifested during the rewarming phase of TTM?

A. Hypokalemia
B. Hypophosphatemia
C. Hyperkalemia
D. Hyperphosphatemia

Question 3

Which of the following options is the most-reasonable first step in the management of TTM-associated shivering?

A. Dexmedetomidine infusion
B. Cisatracurium infusion
C. Active cutaneous counterwarming
D. Propofol infusion
E. Midazolam bolus

Question 4

Which of the following patients would be least appropriate for TTM?

A. 24YO female with asystolic OOHCA secondary to TCA overdose; GCS 5T
B. 84YO male ventricular fibrillation IHCA; GCS 6T
C. 46YO COVID-positive female with ventricular tachycardia IHCA; GCS 5T
D. 39YO male found down at home after unknown downtime with PEA OOHCA; ROSC at 47mins; CT head/brain with loss of gray-white differentiation; GCS2T
E. 69YO female with ventricular fibrillation IHCA after CABG; GCS 7T

Question 5

Which of the following options is NOT a benefit of TTM?

A. Decreased cerebral metabolism
B. Decreased cytokine production
C. Decreased risk of post-arrest shivering
D. Improved post-arrest neurologic outcomes
E. Increased risk of reperfusion injury

References

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