Therapeutic Hypothermia

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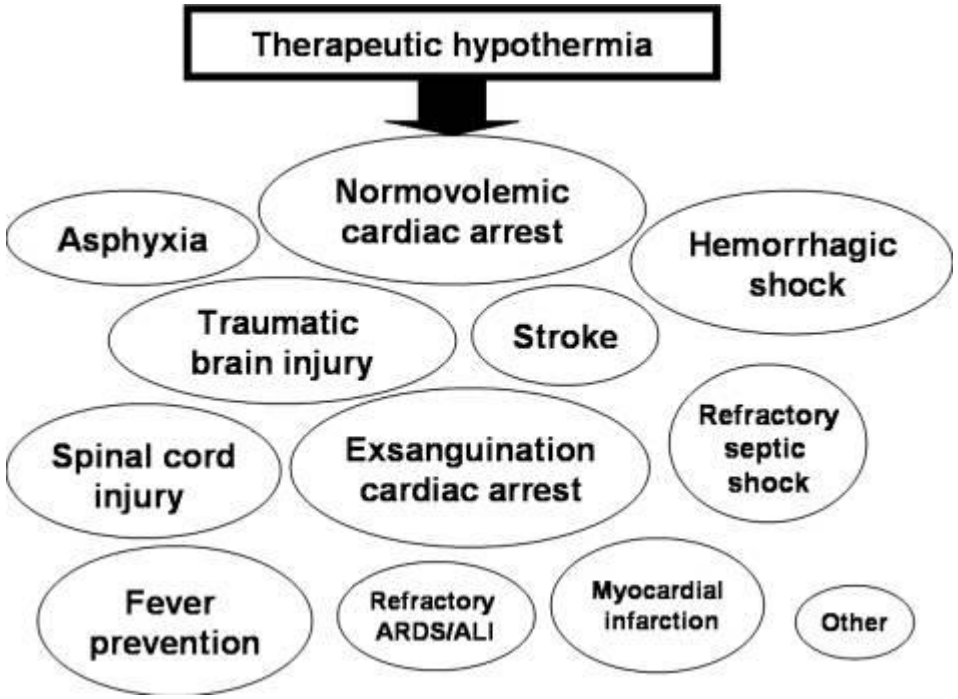
Objectives

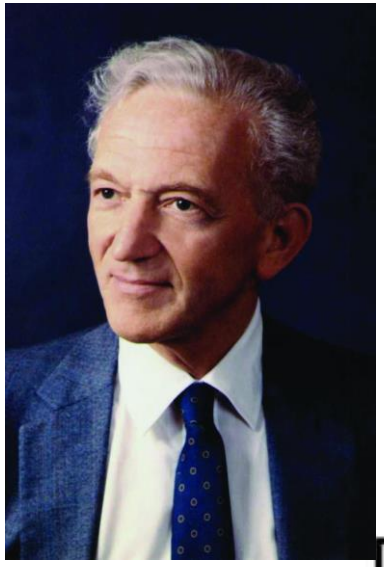
- Brief history of therapeutic hypothermia/Targeted Temp. Management
- Definitions
- Understand some currently available devices
- Review supportive data
- Future directions

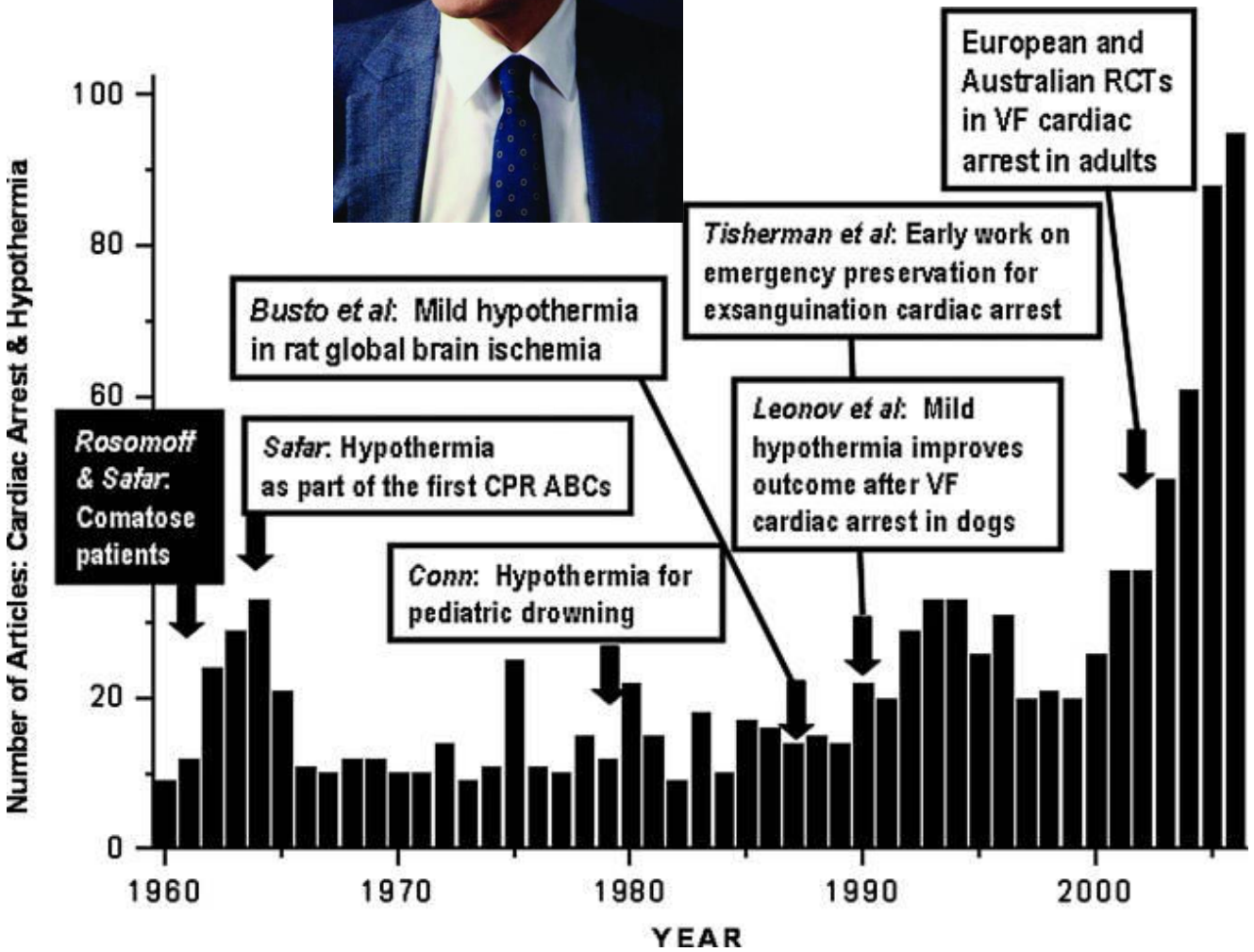
History

- Hypothermia (Hypo- under, therme- heat) – Greek origin
- ‘Some, pale and depressed by inanition, swooned away and died, stretched on the snow … They were seen walking insensible and ignorant where they went … In a word, when no longer able to continue walking, having neither power nor will, they fell on their knees … Their pulse was small and imperceptible; respiration, infrequent and scarcely perceptible in some, was attended in others by complaints and groans. Sometimes the eye was open, fixed, dull, wild, and the brain was seized by quiet delirium.’ -*A Treatise on the Effects and Properties of Cold* (1826) French doctor Pierre Jean Moricheau-Beaupré
- Used by Egyptians, Greeks for millenia to treat infection, hemmorhage

History – Peter Safar



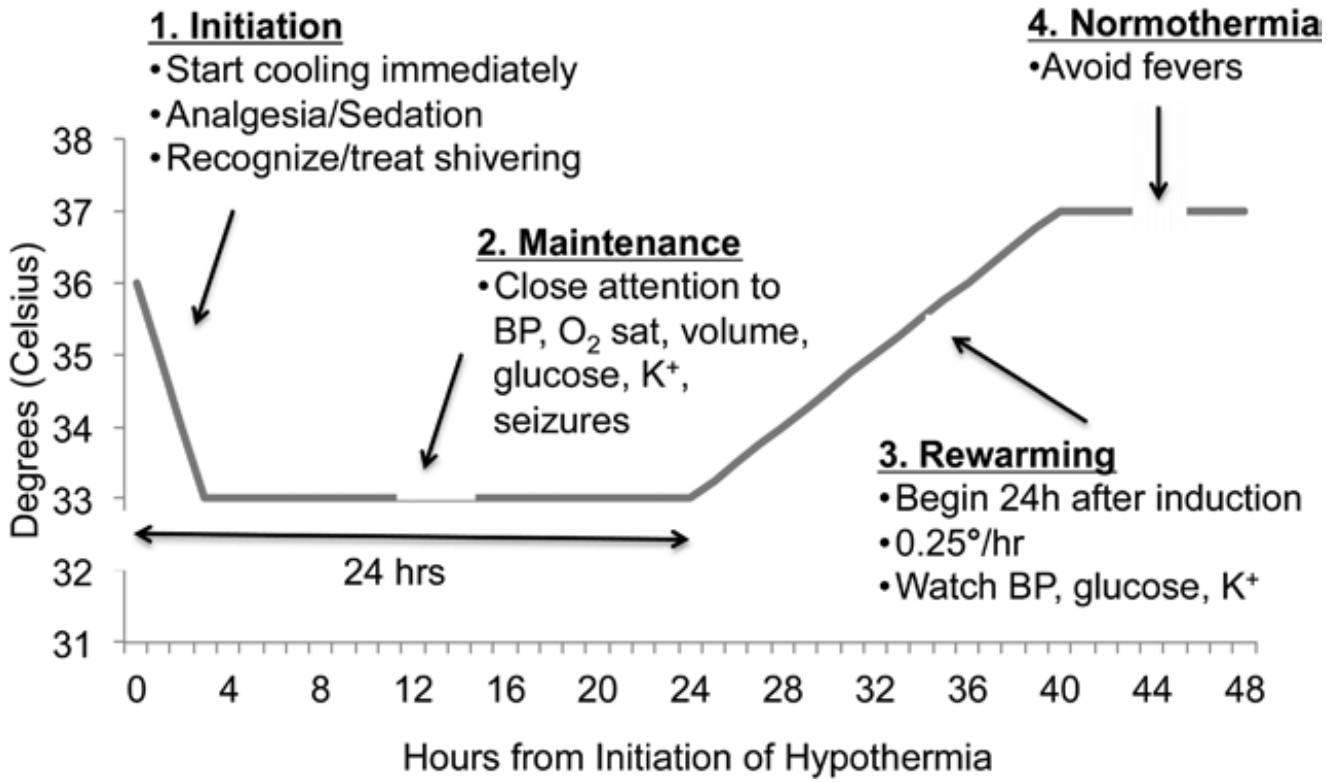


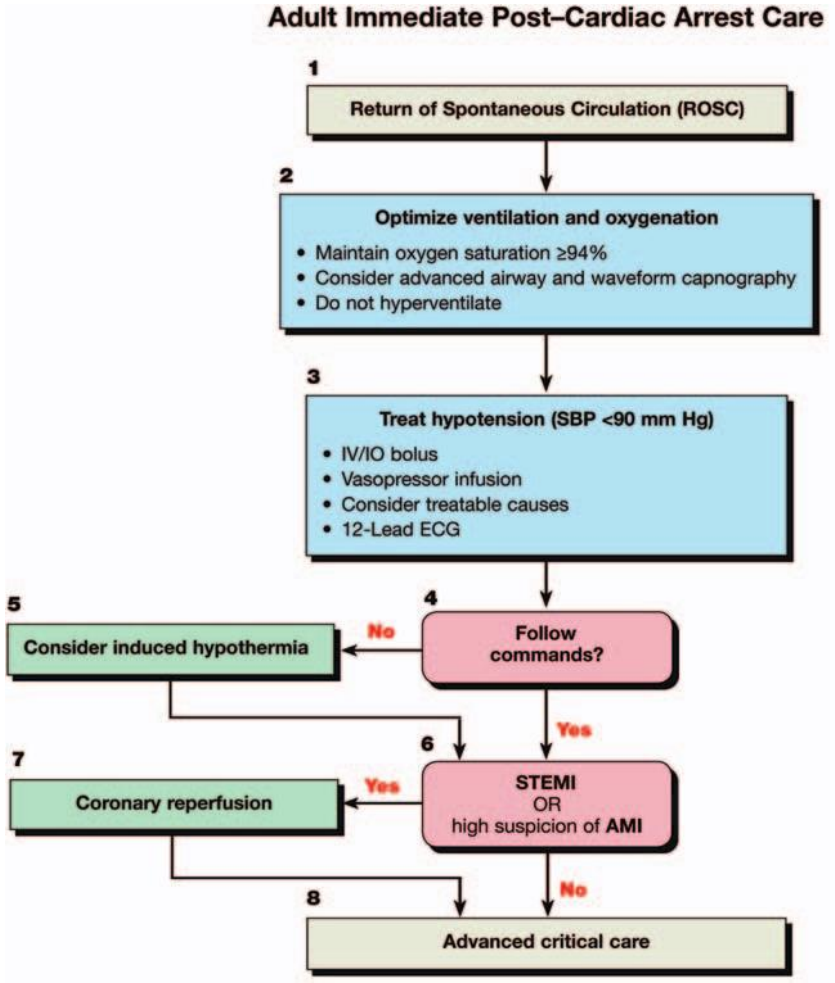


Definition/Mechanisms:

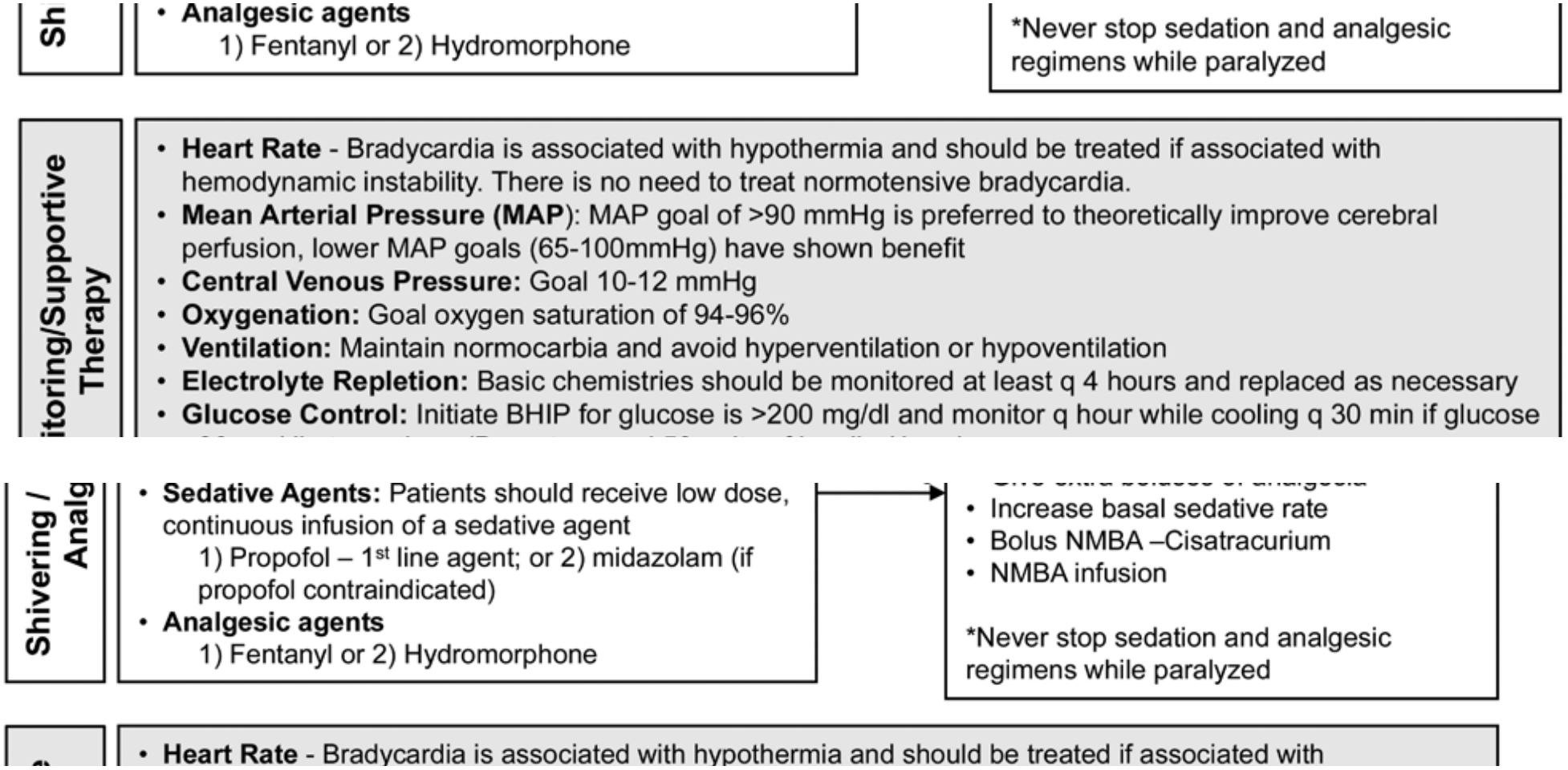
- Mild to moderate hypothermia : 32 to 34 Degrees Celsius
- Neuroprotection/Cardioprotection
  - Decrease in metabolic demand
  - Post ischemia/reperfusion improved
    - Apoptosis, mitochondrial dysfunction, ion pump function
    - Decreased activity of caspase enzyme
    - Decrease in free radical formation

Approach

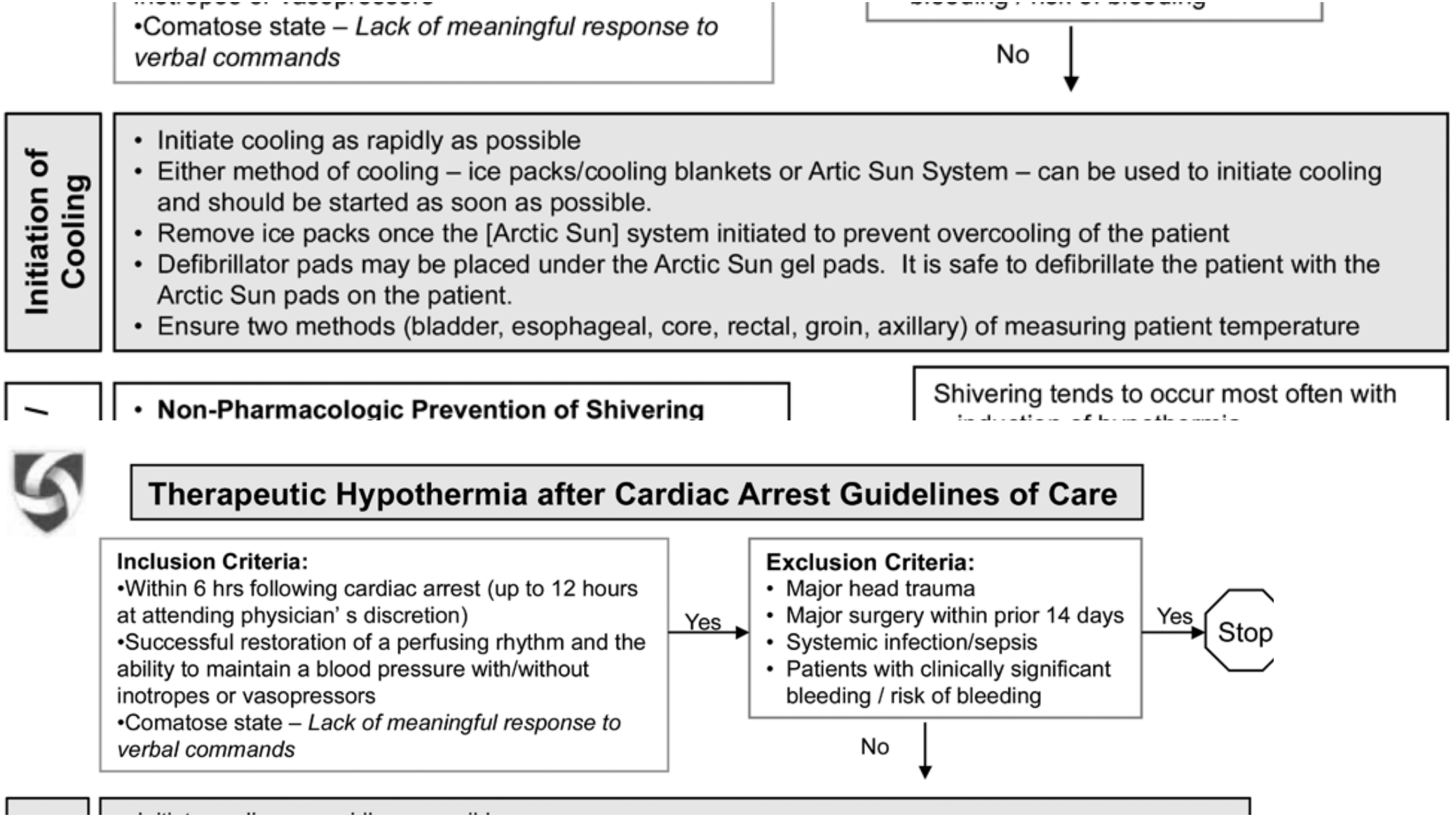

1. Initiation
•Start cooling immediately
•Analgesia/Sedation
•Recognize/treat shivering
2. Maintenance
•Close attention to BP, O_2 sat, volume, glucose, K^+, seizures
3. Rewarming
•Begin 24h after induction
•0.25°/hr
•Watch BP, glucose, K^+
4. Normothermia
•Avoid fevers
24 hrs
Degrees (Celsius)
38
37
36
35
34
33
32
31
0
4
8
12
16
20
24
28
32
36
40
44
48
Hours from Initiation of Hypothermia


Adult Immediate Post–Cardiac Arrest Care
1
Return of Spontaneous Circulation (ROSC)
2
Optimize ventilation and oxygenation
• Maintain oxygen saturation ≥94%
• Consider advanced airway and waveform capnography
• Do not hyperventilate
3
Treat hypotension (SBP <90 mm Hg)
• IV/IO bolus
• Vasopressor infusion
• Consider treatable causes
• 12-Lead ECG
4
Follow commands?
No
5
Consider induced hypothermia
Yes
6
STEMI OR high suspicion of AMI
Yes
7
Coronary reperfusion
No
8
Advanced critical care

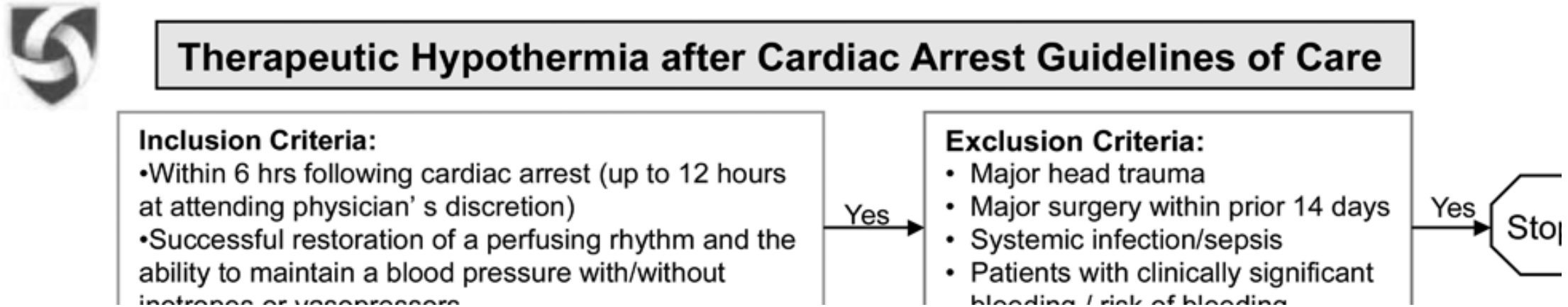
Approach


Sh
• Analgesic agents
1) Fentanyl or 2) Hydromorphone
*Never stop sedation and analgesic regimens while paralyzed
itoring/Supportive Therapy
• Heart Rate - Bradycardia is associated with hypothermia and should be treated if associated with hemodynamic instability. There is no need to treat normotensive bradycardia.
• Mean Arterial Pressure (MAP): MAP goal of >90 mmHg is preferred to theoretically improve cerebral perfusion, lower MAP goals (65-100mmHg) have shown benefit
• Central Venous Pressure: Goal 10-12 mmHg
• Oxygenation: Goal oxygen saturation of 94-96%
• Ventilation: Maintain normocarbia and avoid hyperventilation or hypoventilation
• Electrolyte Repletion: Basic chemistries should be monitored at least q 4 hours and replaced as necessary
• Glucose Control: Initiate BHIP for glucose is >200 mg/dl and monitor q hour while cooling q 30 min if glucose
Shivering / Analg
• Sedative Agents: Patients should receive low dose, continuous infusion of a sedative agent
1) Propofol – 1st line agent; or 2) midazolam (if propofol contraindicated)
• Analgesic agents
1) Fentanyl or 2) Hydromorphone
• Increase basal sedative rate
• Bolus NMBA –Cisatracurium
• NMBA infusion
*Never stop sedation and analgesic regimens while paralyzed
• Heart Rate - Bradycardia is associated with hypothermia and should be treated if associated with

Approach


•Comatose state – Lack of meaningful response to verbal commands
No
Initiation of Cooling
• Initiate cooling as rapidly as possible
• Either method of cooling – ice packs/cooling blankets or Artic Sun System – can be used to initiate cooling and should be started as soon as possible.
• Remove ice packs once the [Arctic Sun] system initiated to prevent overcooling of the patient
• Defibrillator pads may be placed under the Arctic Sun gel pads. It is safe to defibrillate the patient with the Arctic Sun pads on the patient.
• Ensure two methods (bladder, esophageal, core, rectal, groin, axillary) of measuring patient temperature
• Non-Pharmacologic Prevention of Shivering
Shivering tends to occur most often with
Therapeutic Hypothermia after Cardiac Arrest Guidelines of Care
Inclusion Criteria:
•Within 6 hrs following cardiac arrest (up to 12 hours at attending physician' s discretion)
•Successful restoration of a perfusing rhythm and the ability to maintain a blood pressure with/without inotropes or vasopressors
•Comatose state – Lack of meaningful response to verbal commands
Yes
Exclusion Criteria:
• Major head trauma
• Major surgery within prior 14 days
• Systemic infection/sepsis
• Patients with clinically significant bleeding / risk of bleeding
Yes
Stop
No

Approach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Yes
Sto

Available Devices

- Surface cooling – blankets, ice etc
- Adhesive cooling pads – “Arctic Sun”
- Deltatherm – Air cooling
- Cooling helmets – Used in neonates
- Large volume “ice” cold fluid IV infusion
- Drug cooling – Neurotensin analogues
- Endovascular catheter directed cooling
- ECMO circuits

Trials

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

Conclusions In patients who have been successfully resuscitated after cardiac arrest due to ventricular fibrillation, therapeutic mild hypothermia increased the rate of a favorable neurologic outcome and reduced mortality. (N Engl J Med 2002;346:549-56.)

Trials

ORIGINAL ARTICLE

Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm

J.-B. Lascarrou, H. Merdji, A. Le Gouge, G. Colin, G. Grillet, P. Girardie, E. Coupez, P.-F. Dequin, A. Cariou, T. Boulain, N. Brule, J.-P. Frat, P. Asfar, N. Pichon, M. Landais, G. Plantefeve, J.-P. Quenot, J.-C. Chakarian, M. Sirodot, S. Legriel, J. Letheulle, D. Thevenin, A. Desachy, A. Delahaye, V. Botoc, S. Vimeux, F. Martino, B. Giraudeau, and J. Reignier, for the CRICS-TRIGGERSEP Group*

CONCLUSIONS

Among patients with coma who had been resuscitated from cardiac arrest with nonshockable rhythm, moderate therapeutic hypothermia at 33°C for 24 hours led to a higher percentage of patients who survived with a favorable neurologic outcome at day 90 than was observed with targeted normothermia. (Funded by the French Ministry of Health and others; HYPERION ClinicalTrials.gov number, NCT01994772.)

ORIGINAL ARTICLE

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

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D., David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sci., Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D., Jesper Kjaergaard, M.D., D.M.Sci., 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.Sci., John Bro-Jeppesen, M.D., Iole 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 Køber, M.D., D.M.Sci., Jørund Langørgen, M.D., Gisela Lilja, O.T., Jacob Eifer Møller, M.D., D.M.Sci., Malin Rundgren, M.D., Ph.D., Christian Rylander, M.D., Ph.D., Ondrej Smid, M.D., Christophe Werer, M.D., Per Winkel, M.D., D.M.Sci., and Hans Friberg, M.D., Ph.D., for the TTM Trial Investigators*

CONCLUSIONS

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. (Funded by the Swedish Heart–Lung Foundation and others; TTM ClinicalTrials.gov number, NCT01020916.)

Trials

Circulation

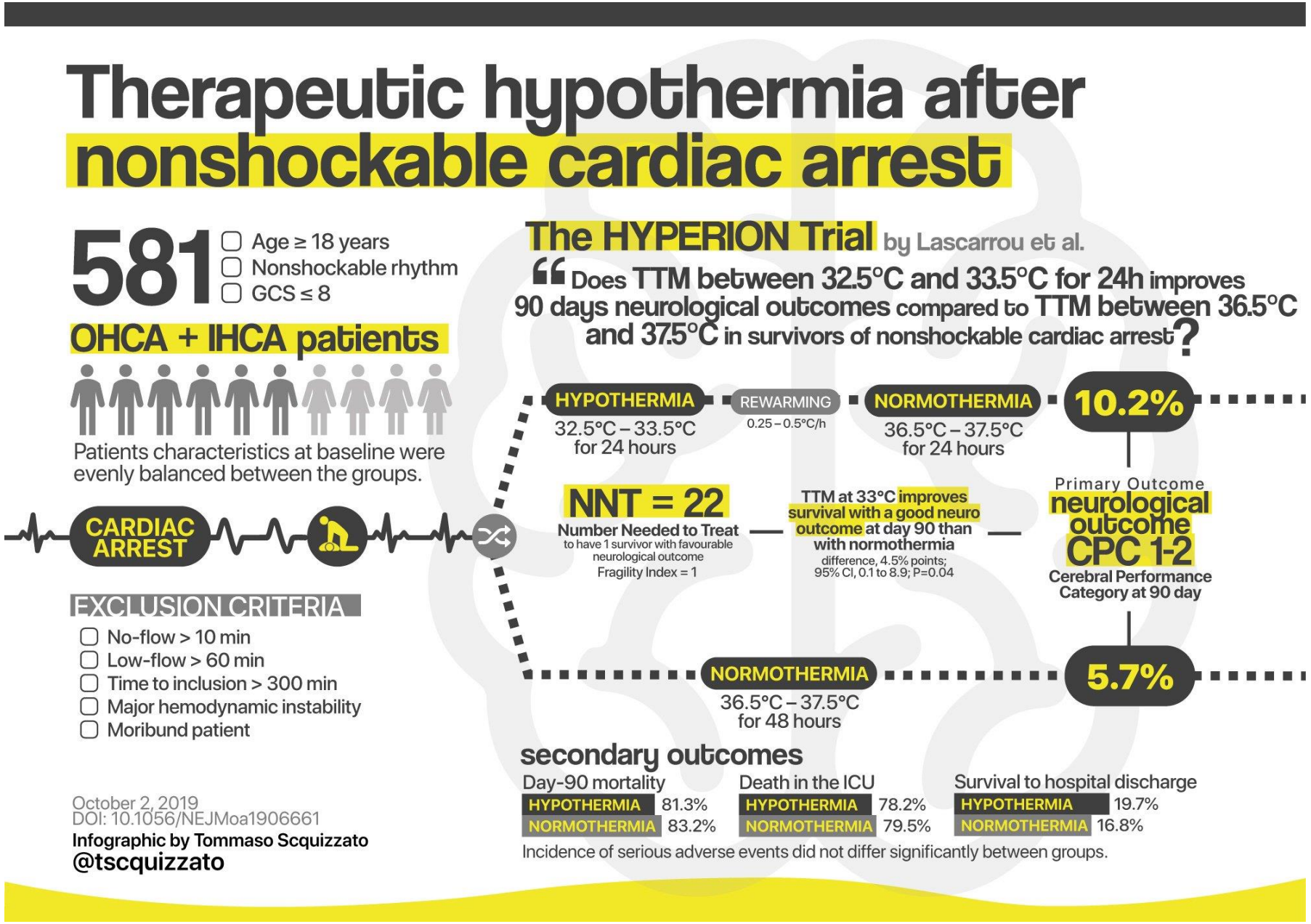
ORIGINAL RESEARCH ARTICLE

Mild Hypothermia in Cardiogenic Shock Complicating Myocardial Infarction

Randomized SHOCK-COOL Trial

CONCLUSIONS: In this randomized trial, mild therapeutic hypothermia failed to show a substantial beneficial effect on cardiac power index at 24 hours in patients with cardiogenic shock after acute myocardial infarction.

Trials


Therapeutic hypothermia after nonshockable cardiac arrest
581
Age ≥ 18 years
Nonshockable rhythm
GCS ≤ 8
OHCA + IHCA patients
Patients characteristics at baseline were evenly balanced between the groups.
CARDIAC ARREST
EXCLUSION CRITERIA
No-flow > 10 min
Low-flow > 60 min
Time to inclusion > 300 min
Major hemodynamic instability
Moribund patient
The HYPERION Trial by Lascarrou et al.
"Does TTM between 32.5°C and 33.5°C for 24h improves 90 days neurological outcomes compared to TTM between 36.5°C and 37.5°C in survivors of nonshockable cardiac arrest?
HYPOTHERMIA
32.5°C – 33.5°C
for 24 hours
REWARMING
0.25 – 0.5°C/h
NORMOTHERMIA
36.5°C – 37.5°C
for 24 hours
10.2%
NNT = 22
Number Needed to Treat
to have 1 survivor with favourable neurological outcome
Fragility Index = 1
TTM at 33°C improves survival with a good neuro outcome at day 90 than with normothermia
difference, 4.5% points;
95% CI, 0.1 to 8.9; P=0.04
Primary Outcome
neurological outcome
CPC 1-2
Cerebral Performance Category at 90 day
NORMOTHERMIA
36.5°C – 37.5°C
for 48 hours
5.7%
secondary outcomes
Day-90 mortality
HYPOTHERMIA 81.3%
NORMOTHERMIA 83.2%
Death in the ICU
HYPOTHERMIA 78.2%
NORMOTHERMIA 79.5%
Survival to hospital discharge
HYPOTHERMIA 19.7%
NORMOTHERMIA 16.8%
Incidence of serious adverse events did not differ significantly between groups.
October 2, 2019
DOI: 10.1056/NEJMoa1906661
Infographic by Tommaso Scquizzato
@tscquizzato

Guideline Recommendations

Temperature Management After Cardiac Arrest
An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation☆

Michael W. Donnino, Lars W. Andersen, Katherine M. Berg, Joshua C. Reynolds, Jerry P. Nolan, Peter T. Morley, Eddy Lang, Michael N. Cocchi, Theodoros Xanthos, Clifton W. Callaway[1], Jasmeet Soar[1], the ILCOR ALS Task Force

- We recommend targeted temperature management as opposed to no targeted temperature management for adults with OHCA with an initial shockable rhythm who remain unresponsive after ROSC (strong recommendation, low-quality evidence).

Future Directions

- Continued treatment of hypoxic ischemic encephalopathy

67th International Astronautical Congress (IAC), Guadalajara, Mexico, 26-30 September 2016.

IAC-16-B3.7.10

A Feasible, Near-Term Approach to Human Stasis for Long-Duration Deep Space Missions

Mark Schaffer [a], John Bradford, Ph.D. [b]., Doug Talk, M.D. [c]

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