Evidence based and Practical points in Neurocritical care

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Scope

- TTM after cardiac arrest
  - Main idea
  - Methods
  - Update
- TTM in Ischemic Stroke
- TTM in Traumatic Brain Injury
- TTM in Kidney Transplantation
- Prognostication after cardiac arrest

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Targeted Temperature Management in Neurological ICU

3

Targeted temperature management in critical care: A report and recommendations from five professional societies*

Mark E. Nunnally, MD; Roman Jaeschke, MD; Geoffrey J. Bellingan, MD; Jacques Lacroix, MD; Bruno Mourvillier, MD; Gloria M. Rodriguez-Vega, MD, FCCM; Sten Rubertsson, MD, PhD, FCCM; Theodoros Vassilakopoulos, MD; Craig Weinert, MD; Sergio Zanotti-Cavazzoni, MD; Timothy G. Buchman, MD, PhD, FCCM

Sponsoring Organizations: American Thoracic Society (ATS) (http://www.thoracic.org), European Respiratory Society (ERS) (http://www.ersnet.org), European Society of Intensive Care Medicine (ESICM) (http://www.esicm.org), Society of Critical Care Medicine (SCCM) (http://www.sccm.org), Société de Réanimation de Langue Française (SRLF) (http://www.srlf.org).

The jury opines that the term "targeted temperature management" replace "therapeutic hypothermia."

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Purpose of TH in Critical care Neurology

- Neuroprotective Therapy
- Decrease ICP

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Theory

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Hypoxic/Ischemic cascade

- Lack of O_2 → no ATP for energy.
- Cell switches to anaerobic metabolism, producing lactic acid.
- ATP-reliant ion transport pumps fail → cell depolarized, allowing Ca^{++} influx.
- ↑ intracellular calcium → release of the excitatory neurotransmitter glutamate
- Stimulates AMPA and NMDA receptors

Muengtaweepongsa S, Srivilaithon W. World J Methodol. 2017 Jun 26;7(2):55-67

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Hypoxic/Ischemic cascade (2)

- ↑ free radicals, reactive O_2 species, excitotoxicity (endonucleases, ATPases, and phospholipases)
- Cell's membrane & Mitochondria broken down by phospholipases
- Cell dies through necrosis → glutamate into environment → poison nearby neurons

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Reperfusion Injury

- An inflammatory response is mounted, and phagocytic cells engulf damaged but still viable tissue
- Harmful chemicals damage BBB
- Cerebral edema due to leakage of large molecules like albumins from vessels through the damaged BBB → pull water into brain tissue by osmosis (vasogenic edema) → compression brain tissue

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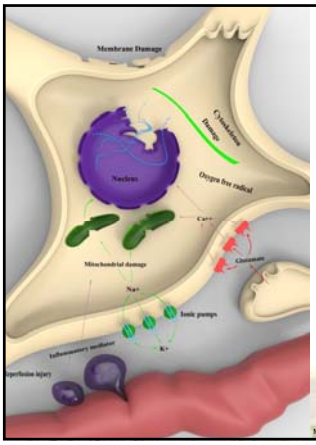

Ischemic cascade

Thank you Jennarong Muengtaweepongsa

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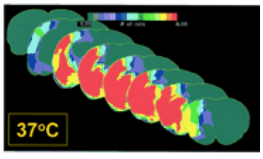
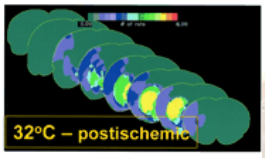
Hypothermia





Stroke. 2003;34:214-223

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Mechanisms of neuroprotection by hypothermia

- counteract ischemic brain damage by several mechanisms
  - prevention of the blood–brain-barrier disruption
  - ⇓ oxygen-based free-radical production
  - ⇓ excitotoxicneurotransmitter release
  - anti-inflammatory action
  - delayed apoptosis

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ILCOR Advisory Statement

Therapeutic Hypothermia After Cardiac Arrest

An Advisory Statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation

Writing Group

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Additional Contributors

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2005 ILCOR

- **There seems to be good evidence (level 1) to recommend the use of induced mild hypothermia in comatose survivors of-out-hospital cardiac arrest caused by VF.**

Level 1 evidence indicates one or more randomized clinical trials in which benefit was shown

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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association. Learn and Live.

Part 9: Post Cardiac Arrest Care: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Mary Ann Peberdy, Clifton W. Callaway, Robert W. Neumar, Romergryko G. Geocadin, Janice L. Zimmerman, Michael Donnino, Andrea Gabrielli, Scott M. Silvers, Arno L. Zaritsky, Raina Merchant, Terry L. Vanden Hoek and Steven L. Kronick

Circulation 2010;122:S768-S786

DOI: 10.1161/CIRCULATIONAHA.110.971002

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PostCardiac Arrest Care: 2010

- In summary, we recommend that 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).

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Therapeutic Hypothermia after Cardiac Arrest

The New England Journal of Medicine

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

(N Engl J Med 2002;346:557-63.)

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.

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The RCT of TH after cardiac arrest

	HACA (European)	Bernard trial (Australia)
Sample	N=275	N=77
Cooled verses normothermia	137 cooled 138 normothermia	43 cooled 34 normothermia
Intervention	Cooling blankets and ice packs	Ice packs
Target temperature	32-34 degrees	33 degrees
Initiation	Prehospital	ER
Duration	24 hours	12 hours
Follow up	6 months	30 days

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Benefit

- **NNT of 7 to prevent 1 death with TH**
- **NNT of 6 to reduce neurologic impairment with TH**

The NNT is the number of patients who need to be treated in order to prevent one additional bad outcome

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Methods of Cooling

- Selective head cooling
  - Cooling helmet: ineffective in adult
- Internal cooling by intravenous and intraarterial ice-cold saline
  - Need large volume
- Surface cooling
- Endovascular cooling

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Surface method of TH

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Surface blanket




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น้ำแข็งชับน้ำตา

การประยุกต์ใช้น้ำแข็ง ใน รพ. เจ้าพระยายมราช



25

น้ำแข็งชับน้ำตา

26 มิถุนายน 2557 ชายไทย อายุ 36 ปี
ไม่รู้สึกตัว 15นาที ก่อนมาโรงพยาบาล

CPR 30 นาที
ได้ adrenaline 20 amp
Defibrillation 200 joule X 3
GCS = 4T





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Surface cooling

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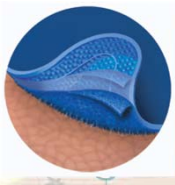
Surface cooling



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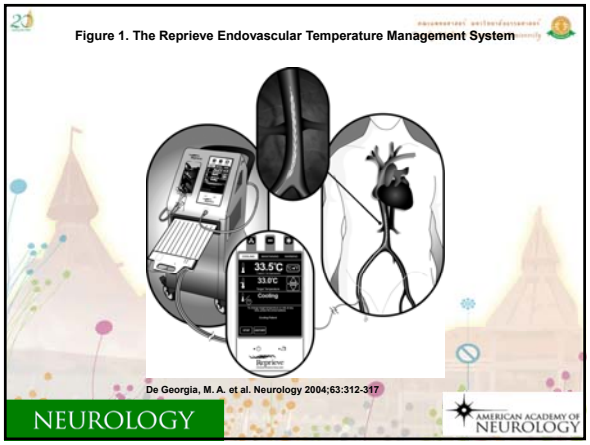

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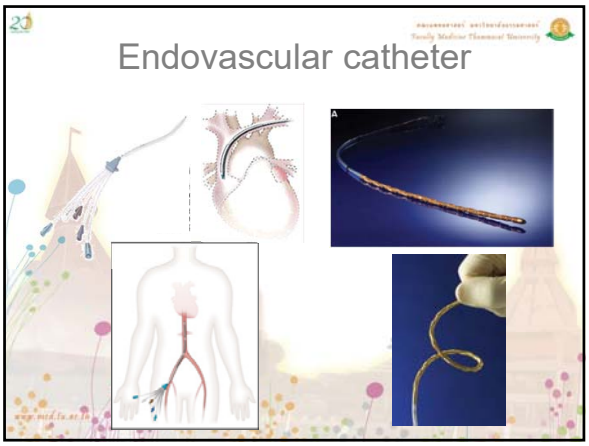

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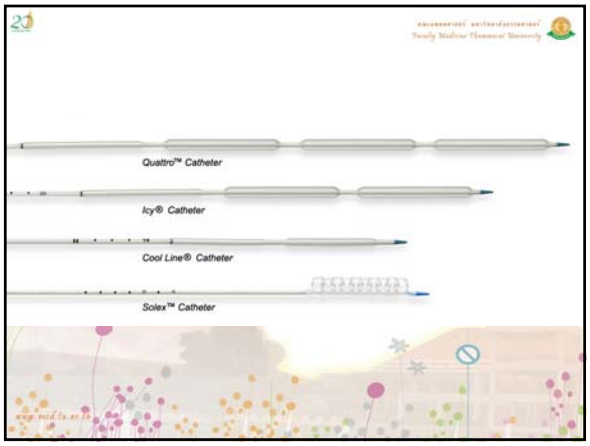

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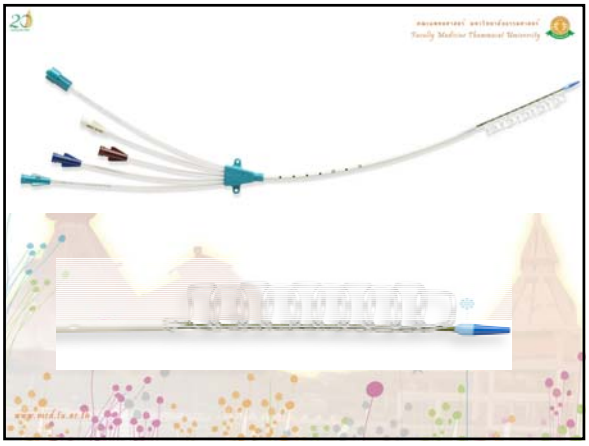

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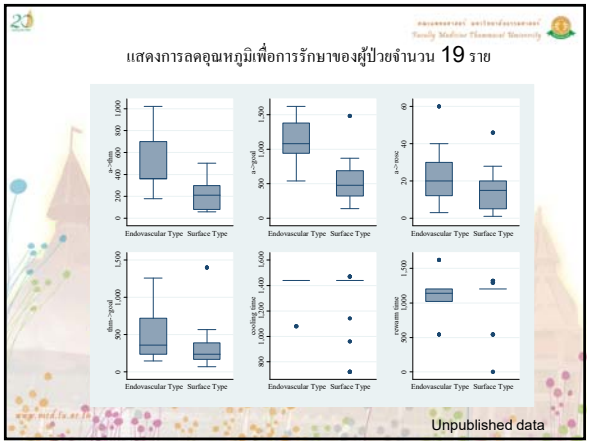

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Site of temperature probe

- PA cath
  - Most accurate but high complication rate
- Esophagus
  - High accuracy but may not comfortable to patient
- Rectum
  - Medium accuracy with lag behind core temp 10 – 15 min. but easy to use

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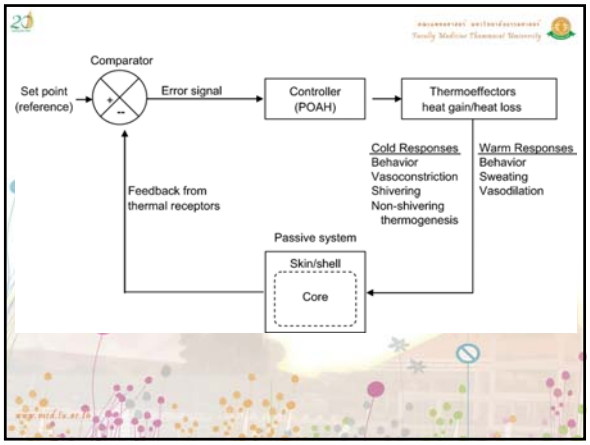

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Bedside Shivering Assessment Score (BSAS)

0	No shivering
1	Mild: Shivering localized to neck and/or thorax only
2	Moderate: Shivering involves gross movement of upper limbs
3	Severe: Shivering involves gross movement of trunk, upper and lower limbs

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Introduction of thermoregulatory tolerance

- Nonpharmacological treatments
  - Skin counterwarming
- Pharmacological treatments
  - Anesthetics and Muscle relaxants
  - Meperidine
  - Drug combination
    - Meperidine and Buspirone
    - Meperidine and Dexmedetomidine

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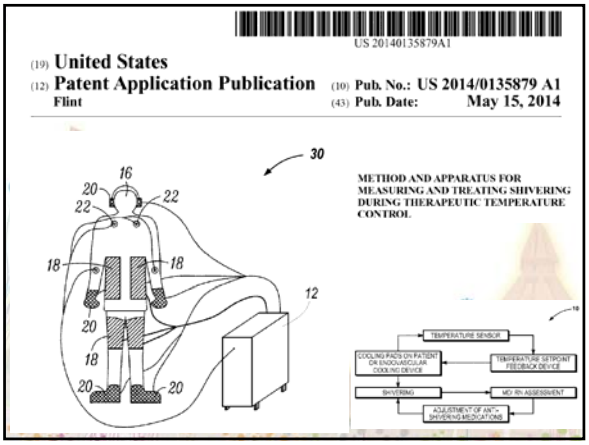

US 20140135879A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2014/0135879 A1**

Flint (43) **Pub. Date: May 15, 2014**

METHOD AND APPARATUS FOR MEASURING AND TREATING SHIVERING DURING THERAPEUTIC TEMPERATURE CONTROL

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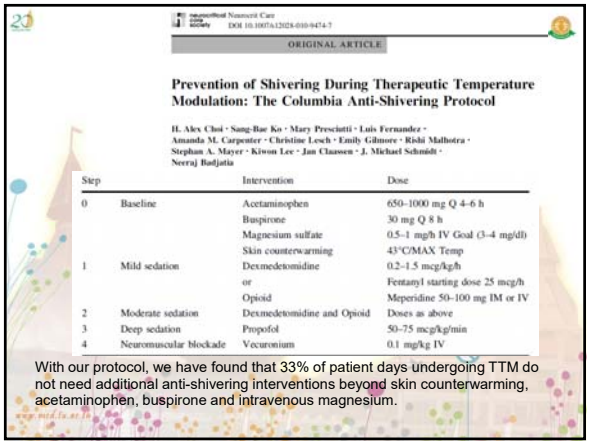

ORIGINAL ARTICLE

Prevention of Shivering During Therapeutic Temperature Modulation: The Columbia Anti-Shivering Protocol

H. Alex Choi · Sang-Bae Ko · Mary Presciutti · Luis Fernandez · Amanda M. Carpenter · Christine Lesch · Emily Gilmore · Rishi Malhotra · Stephan A. Mayer · Kiwon Lee · Jan Claassen · J. Michael Schmidt · Neeraj Badjatia

Step		Intervention	Dose
0	Baseline	Acetaminophen	650–1000 mg Q 4–6 h
		Buspirone	30 mg Q 8 h
		Magnesium sulfate	0.5–1 mg/h IV Goal (3–4 mg/dl)
		Skin counterwarming	43°C/MAX Temp
1	Mild sedation	Dexmedetomidine	0.2–1.5 mcg/kg/h
		or	Fentanyl starting dose 25 mcg/h
		Opioid	Meperidine 50–100 mg IM or IV
2	Moderate sedation	Dexmedetomidine and Opioid	Doses as above
3	Deep sedation	Propofol	50–75 mcg/kg/min
4	Neuromuscular blockade	Vecuronium	0.1 mg/kg IV

With our protocol, we have found that 33% of patient days undergoing TTM do not need additional anti-shivering interventions beyond skin counterwarming, acetaminophen, buspirone and intravenous magnesium.

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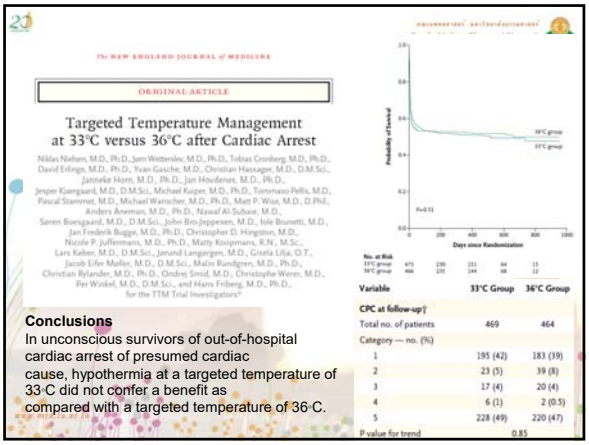

THE NEW ENGLAND JOURNAL of MEDICINE

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 Aneman, 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 Langorgen, 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.

Variable	33°C Group	36°C Group
CPC at follow-up†		
Total no. of patients	469	464
Category — no. (%)		
1	195 (42)	183 (39)
2	23 (5)	39 (8)
3	17 (4)	20 (4)
4	6 (1)	2 (0.5)
5	228 (49)	220 (47)
P value for trend		0.83

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CPC category	Description
1	Conscious and alert with normal function or only slight disability
2	Conscious and alert with moderate disability
3	Conscious with severe disability
4	Comatose or persistent vegetative state
5	Brain dead or death from other causes

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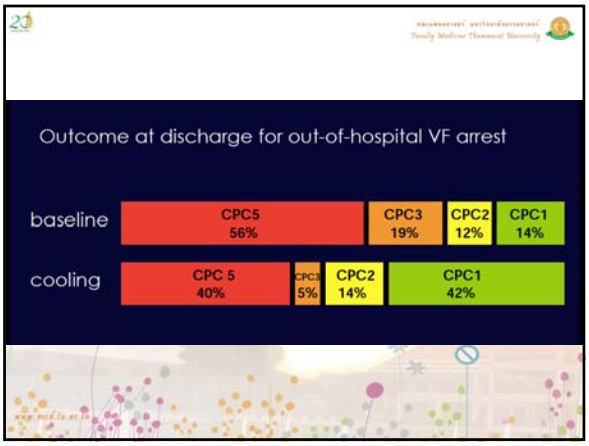

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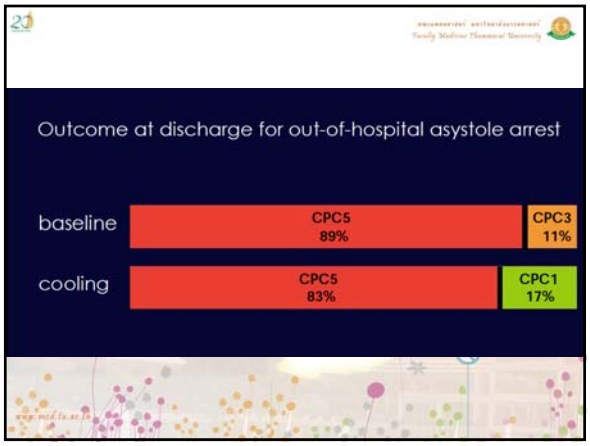

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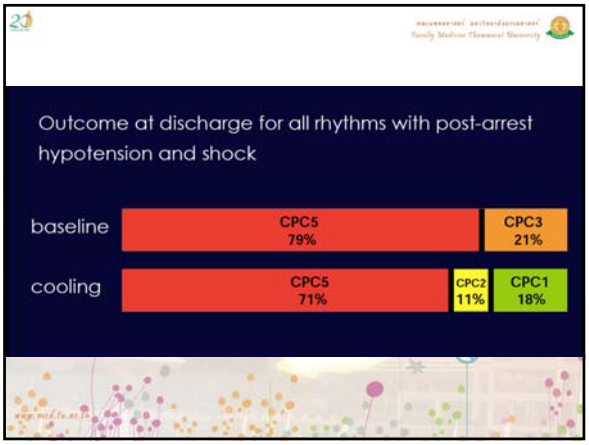

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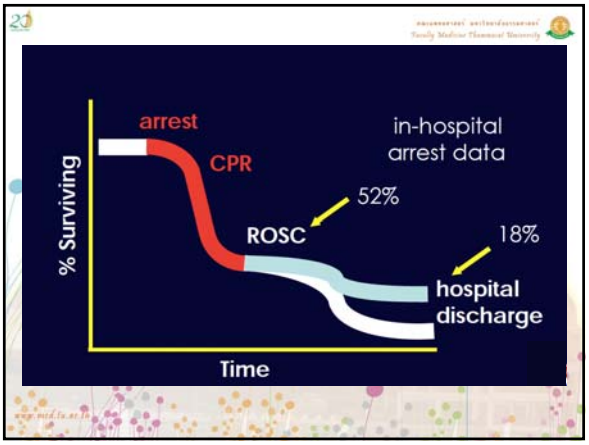

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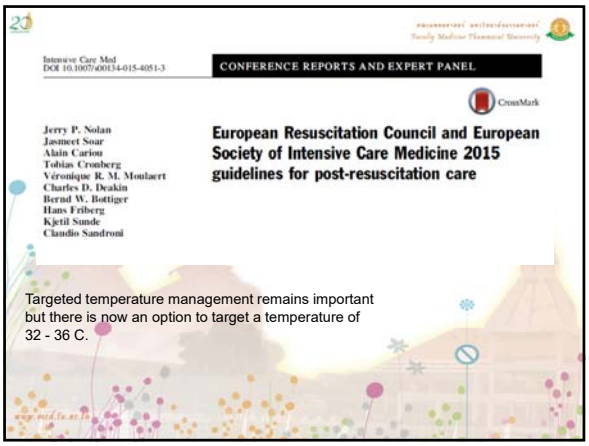

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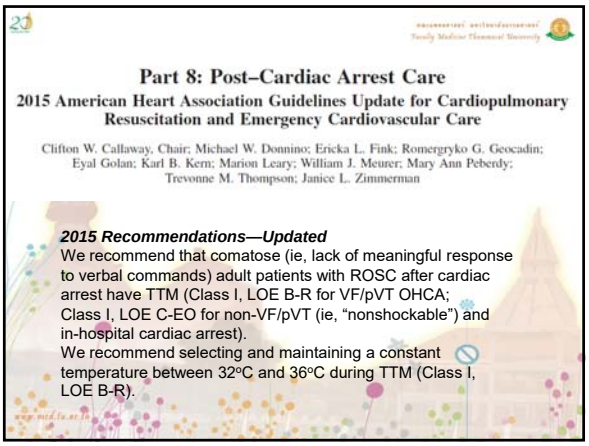

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ILCOR 2015 (1)

- For patients who remain comatose after return of spontaneous circulation (ROSC), should targeted temperature management be used?
  - We *recommend targeted temperature management as opposed to no targeted temperature management for adults with OHCA / IHCA with an initial shockable / nonshockable rhythm who remain unresponsive after ROSC*

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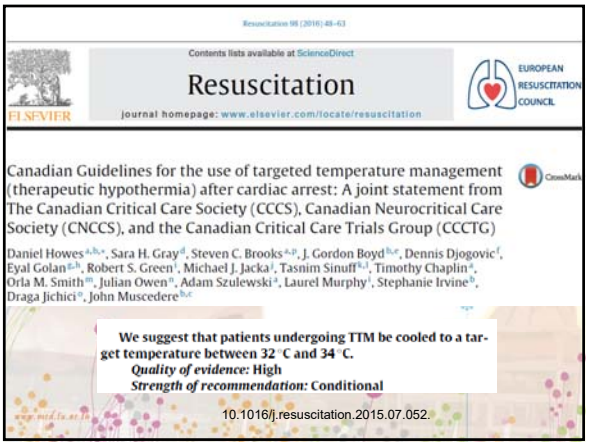

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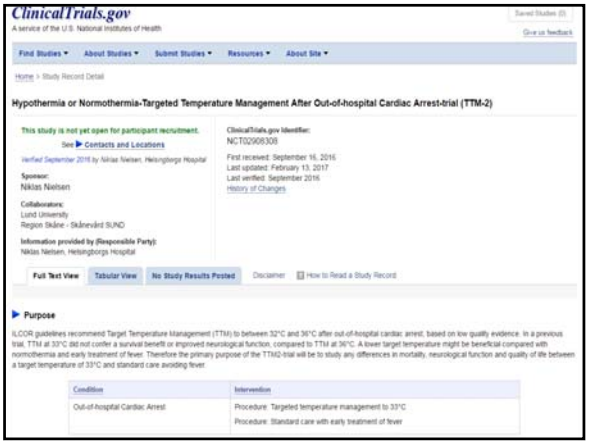

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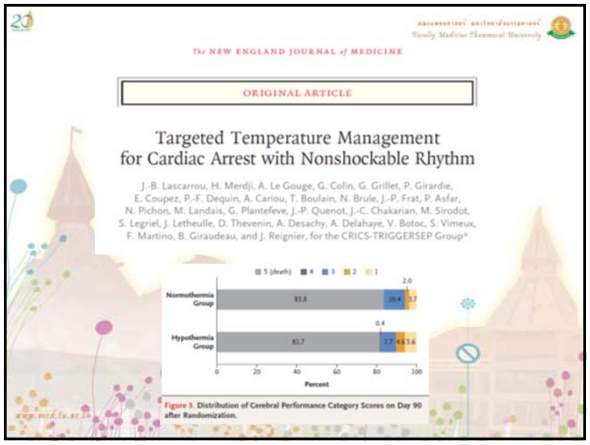

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Therapeutic Hypothermia after Cardiac Arrest

- Class I recommendation
  - In adult
  - In children ?
- "Time is Brain"
- Ideal Temperature Pattern
  - Multimodality of method
- Target temperature ??? (TTM not TH)
  - 33 to 36 ºC

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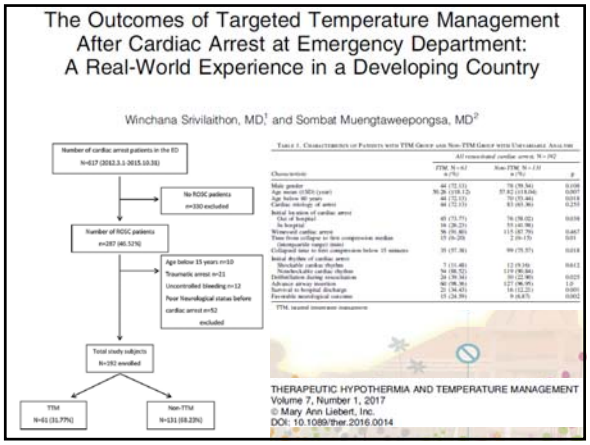

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TTM for Ischemic Stroke

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A case scenario

59 y/o man presented to an outside hospital with sudden onset of right sided weakness and speech impairment. He arrived at the OSH at 90 minutes after onset. CT-brain was negative. He was transferred to our hospital. The i.v. rt-PA was started at 180 minutes after the onset.

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A case scenario (cont.)

He was alert and awake, but aphasic.
NIHSS was 14 with:
- LOCb 2, LOCc 2
- partial hemianopia,
- right arm weakness,
- some effort against gravity on right leg,
- partial sensory loss on the left side
- Severe aphasia.

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A case scenario (cont.)

Without either intubation or sedation, therapeutic hypothermia with Arctic Sun was started at 8 hours after onset. Target core temperature of 33°C was reached within 5 hrs. Shivering was under control with combination of surface counterwarming and meperidine plus fentanyl. Gradual rewarming was applied after target temperature was maintained for 24 hrs.

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He was discharged with home rehab after 12 days of admission with NIHSS of 7 and mRS of 3.

At 3 months, he walked by himself to follow up at OPD. NIHSS was only 5 including mod aphasia, partial hemianopia and partial sensory loss. mRS was 2.

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Results of the ICTuS 2 Trial (Intravascular Cooling in the Treatment of Stroke 2)

Patrick Lyden, MD; Thomas Hemmen, MD, PhD; James Grotta, MD; Karen Rapp, BSN; Karin Ernstrom, MS; Teresa Rzesiewicz, MSN; Stephanie Parker, MSN; Mauricio Concha, MD; Syed Hussain, MD; Sachin Agarwal, MD; Brett Meyer, MD; Julie Jurf, MSN; Irfan Altafullah, MD; Rema Raman, PhD

Background and Purpose—Therapeutic hypothermia is a potent neuroprotectant approved for cerebral protection after neonatal hypoxia-ischemia and cardiac arrest. Therapeutic hypothermia for acute ischemic stroke is safe and feasible in pilot trials. We designed a study protocol to provide safer, faster therapeutic hypothermia in stroke patients.

Methods—Safety procedures and 4°C saline infusions for faster cooling were added to the ICTuS trial (Intravascular Cooling in the Treatment of Stroke) protocol. A femoral venous intravascular cooling catheter after intravenous recombinant tissue-type plasminogen activator in eligible patients provided 24 hours cooling followed by a 12-hour rewarm. Serial safety assessments and imaging were performed. The primary end point was 3-month modified Rankin score 0,1.

Results—Of the intended 1600 subjects, 120 were enrolled before the study was stopped. Randomly, 63 were to receive hypothermia plus antishivering treatment and 57 normothermia. Compared with previous studies, cooling rates were improved with a cold saline bolus, without fluid overload. The intention-to-treat primary outcome of 90-day modified Rankin Score 0,1 occurred in 33% hypothermia and 38% normothermia subjects, odds ratio (95% confidence interval) of 0.81 (0.36–1.85). Serious adverse events occurred equally. Mortality was 15.9% hypothermia and 8.8% normothermia subjects, odds ratio (95% confidence interval) of 1.95 (0.56–7.79). Pneumonia occurred in 19% hypothermia versus 10.5% in normothermia subjects, odds ratio (95% confidence interval) of 1.99 (0.63–6.98).

Conclusions—Intravascular therapeutic hypothermia was confirmed to be safe and feasible in recombinant tissue-type plasminogen activator–treated acute ischemic stroke patients. Protocol changes designed to reduce pneumonia risk appeared to fail, although the sample is small.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01123161.

(*Stroke*. 2016;47:2888-2895. DOI: 10.1161/STROKEAHA.116.014200.)

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Therapeutic Hypothermia After Recanalization in Patients With Acute Ischemic Stroke

Ji Man Hong, MD, PhD; Jin Soo Lee, MD, PhD; Hee-Jung Song, MD; Hye Seon Jeong, MD; Huimahn Alex Choi, MD; Kiwon Lee, MD

Background and Purpose—Therapeutic hypothermia improves outcomes in experimental stroke models, especially after ischemia-reperfusion injury. We investigated the clinical and radiological effects of therapeutic hypothermia in acute ischemic stroke patients after recanalization.

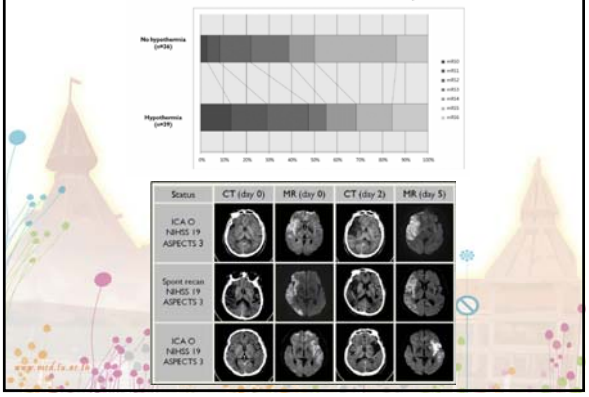
Methods—A prospective cohort study at 2 stroke centers was performed. We enrolled patients with acute ischemic stroke in the anterior circulation with an initial National Institutes of Health Stroke Scale ≥10 who had successful recanalization (2thrombolysis in cerebral ischemia, 2b). Patients at center A underwent a mild hypothermia (34.5°C) protocol, which included mechanical ventilation, and 48-hour hypothermia and 48-hour rewarming. Patients at center B were treated according to the guidelines without hypothermia. Cerebral edema, hemorrhagic transformation, good outcome (3-month modified Rankin Scale, ≤2), mortality, and safety profiles were compared. Potential variables at baseline and during the therapy were analyzed to evaluate for independent predictors of good outcome.

Results—The hypothermia group (n=39) had less cerebral edema (P=0.001), hemorrhagic transformation (P=0.016), and better outcome (P=0.017) compared with the normothermia group (n=36). Mortality, hemicraniectomy rate, and medical complications were not statistically different. After adjustment for potential confounders, therapeutic hypothermia (odds ratio, 3.0; 95% confidence interval, 1.0–8.9; P=0.047) and distal occlusion (odds ratio, 7.3; 95% confidence interval; 1.3–40.3; P=0.022) were the independent predictors for good outcome. Absence of cerebral edema (odds ratio, 5.4; 95% confidence interval, 1.6–18.2; P=0.006) and no medical complications (odds ratio, 9.3; 95% confidence interval, 2.2–39.9; P=0.003) were also independent predictors for good outcome during the therapy.

Conclusions—In patients with ischemic stroke, after successful recanalization, therapeutic hypothermia may reduce risk of cerebral edema and hemorrhagic transformation, and lead to improved clinical outcomes. (*Stroke*. 2014;45:134-140.)

Key Words: hypothermia ■ ischemia ■ ischemic ■ neuroprotection ■ reperfusion injury ■ stroke

67



68

EuroHYP-1 treatment

Cooling will be maintained at 34–35◦C for 24 h with a surface or endovascular technique.

69

EuroHYP-1

European multicentre, randomised, phase III clinical trial of therapeutic hypothermia plus best medical treatment versus best medical treatment alone for acute ischaemic stroke

To determine whether systemic cooling to a target body temperature between 34.0 and 35.0°C, started within 6 hours of symptom onset and maintained for 24 hours, improves functional outcome at 3 months in patients with acute ischaemic stroke.

Chief Investigator: Prof. Dr. med. Dr. h.c. Stefan Schwab
Number and location of participating sites (by region/ country): Currently Centres in Germany, Belgium, Denmark, UK, France, Italy, Spain and Turkey

Funder: Seventh Framework Programme (FP7) of the European Union (Grant Agreement no. 278709).
Start and End date of grant award of recruitment: July 2013 - March 2017

Current Status: awaiting publication

Website: http://www.eurohyp1.eu/

Trial Unblinding Information: Unblinding will only happen after all analyses are finalised and two unbiased conclusions have been written, one assuming that one group is the hypothermia group and the other assuming that the same group is the normothermia group.

Contact details : University Hospital Erlangen
Represented by the Dean at Medical Faculty, Friedrich-Alexander-Universität Erlangen-Nürnberg, Maximiliansplatz 2, 91054 Erlangen

ECTU Involvement: eCRF and Database

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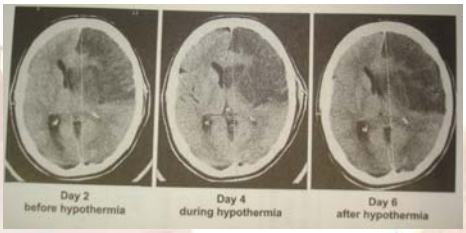
Hypothermia for Malignant MCA Infarction

71



72

Application of TTM in Traumatic Brain Injury (TBI)

73

TTM in animal model with TBI

- **Protective effects of TTM against neurometabolic cascade of TBI were proved with many studies in animal models.**
- **The leakage of endogenous vascular proteins from the disrupted BBB was reduced with hypothermia = ↓ ICP**

74

Clinical trials of TTM in patients with TBI

75

The New England Journal of Medicine

LACK OF EFFECT OF INDUCTION OF HYPOTHERMIA AFTER ACUTE BRAIN INJURY

Guy L. Clifton, M.D., Emmy R. Miller, Pharm.D., R.N., Sung C. Choi, Ph.D., Harvey S. Levin, Ph.D., Stephen McCauley, Ph.D., Kenneth R. Smith, Jr., M.D., J. Paul Muizelaar, M.D., Ph.D., Franklin C. Wagner, Jr., M.D., Donald W. Marion, M.D., Thomas G. Luerssen, M.D., Randall M. Chesnut, M.D., and Michael Schwartz, M.D.

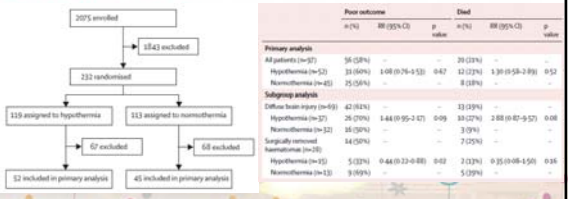
Results The mean age of the patients and the type and severity of injury in the two treatment groups were similar. The mean (±SD) time from injury to randomization was 4.3±1.1 hours in the hypothermia group and 4.1±1.2 hours in the normothermia group, and the mean time from injury to the achievement of the target temperature of 33°C in the hypothermia group was 8.4±3.0 hours. The outcome was poor (defined as severe disability, a vegetative state, or death) in 57 percent of the patients in both groups. Mortality was 28 percent in the hypothermia group and 27 percent in the normothermia group (P=0.79). The patients in the hypothermia group had more hospital days with complications than the patients in the normothermia group. Fewer patients in the hypothermia group had high intracranial pressure than in the normothermia group.

Conclusions Treatment with hypothermia, with the body temperature reaching 33°C within eight hours after injury, is not effective in improving outcomes in patients with severe brain injury. (N Engl J Med 2001; 344:556-63.)

76

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

Guy L Clifton, Alex Valadka, David Zygun, Christopher S Coffey, Pamala Drever, Sierra Fourwinds, L Scott Janis, Elizabeth Wilde, Pauline Taylor, Kathy Harshman, Adam Conley, Ava Puccio, Harvey S Levin, Stephen R McCauley, Richard D Bucholz, Kenneth R Smith, John H Schmidt, James N Scott, Howard Yonas, David O Okonkwo



Interpretation This trial did not confirm the utility of hypothermia as a primary neuroprotective strategy in patients with severe traumatic brain injury.

Lancet Neurol 2011; 10: 131–39

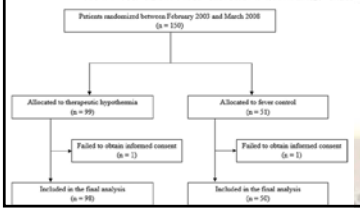
77

JOURNAL OF NEUROTRAUMA 32:422–429 (April 1, 2015)
© Mary Ann Liebert, Inc.
DOI: 10.1089/neu.2013.3197

Original Articles

Prolonged Mild Therapeutic Hypothermia versus Fever Control with Tight Hemodynamic Monitoring and Slow Rewarming in Patients with Severe Traumatic Brain Injury: A Randomized Controlled Trial

Tsuyoshi Maekawa,[1,2,*] Susumu Yamashita,[2,*] Seigo Nagao,[3] Nariyuki Hayashi,[4] and Yasuo Ohashi[5] on behalf of the Brain-Hypothermia (B-HYPO) Study Group[†]



We concluded that tight hemodynamic management and slow rewarming, together with prolonged therapeutic hypothermia (32–34C) for severe TBI, did not improve the neurological outcomes or risk of mortality compared with strict temperature control (35.5–37C).

78

TTM and ICP in TBI

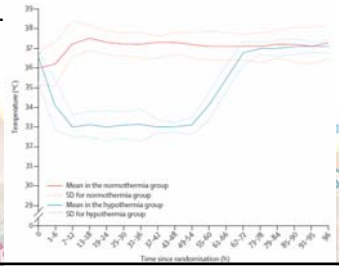
79

ICP is a strong predictor of outcome from severe TBI

80

Pitfalls of previous trials in ICP

- Most trials began rewarming patients after a pre-determined length of time regardless of ICP.



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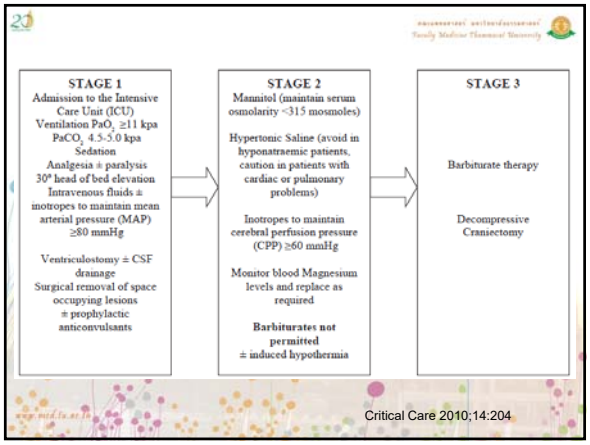

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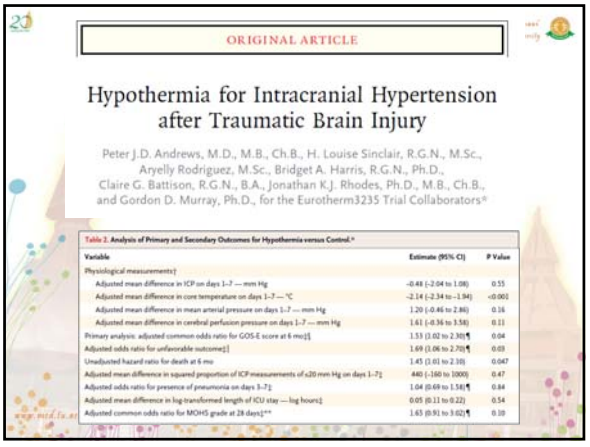

83

TTM in TBI

- **Neurometabolic cascade is a key of primary pathologic damage in TBI.**
- **Available methods for TTM are feasible and effective to apply in TBI.**
- **Absolute benefit is still controversial for TTM in patients with TBI due to lack of evidence from large scale clinical trials.**

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Conclusion

- The main purpose of TTM is neuroprotection
- TTM is ***a standard treatment*** in selected patients after cardiac arrest.
- TTM should be benefit for penumbra salvaging / reperfusion defense in acute ischemic stroke.
- TTM is one of treatment options for increase ICP.

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World Journal of Methodology

Targeted temperature management in neurological intensive care unit

87


Chapter 12

Targeted Temperature Management in Traumatic Brain Injury

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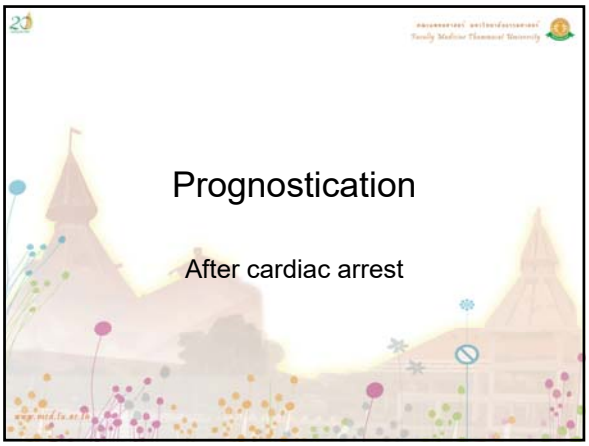
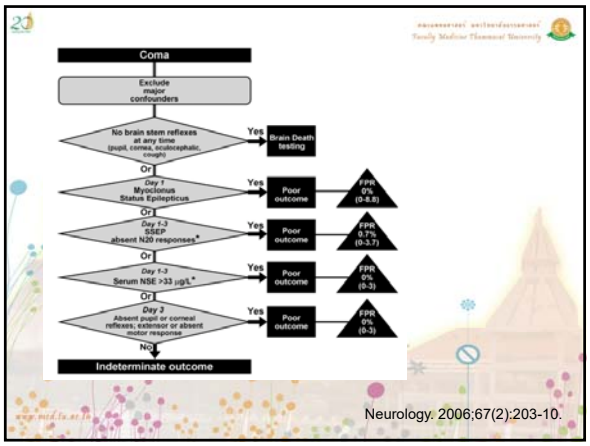

Prognostication

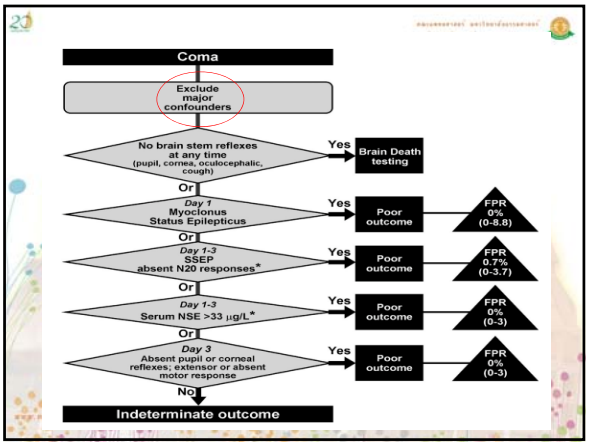
After cardiac arrest

89



Neurology. 2006;67(2):203-10.

90



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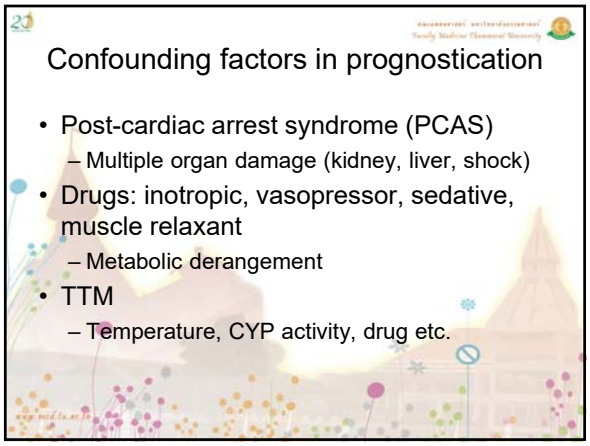
Confounding factors in prognostication

- Post-cardiac arrest syndrome (PCAS)
  - Multiple organ damage (kidney, liver, shock)
- Drugs: inotropic, vasopressor, sedative, muscle relaxant
  - Metabolic derangement
- TTM
  - Temperature, CYP activity, drug etc.

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Neurological Examination

Mandatory and Practical

But interfered by many confounders

97

Assessment of Brainstem Reflexes

- Absence of pupillary or corneal reflex at 72 hrs → poor outcomes (0% false-positive rate) in pt without TTM
- After TTM 72 hrs absence of pupillary reflex still → poor outcomes (0% false-positive rate)
- But some absence of corneal reflex at 72 hrs after TTM → good outcomes (5% FPR)

Prognosis of Coma After Cardiac Arrest in the Era of Therapeutic Hypothermia.
De Georgia, Michael, Raad, Bassel

CONTINUUM: Lifelong Learning in Neurology. 18(3) Critical Care Neurology 515-531, June 2012.
DOI: 10.1212/01.CON.0000415425.68900.c6

99

Assessment of the Best Motor Response

- absent motor response or the presence of decerebrate at 72 hrs → poor outcomes (FPR 0%)
- After TTM at 72 hrs absent motor response or the presence of decerebrate may have good outcomes (FPR 5 – 24%)

Prognosis of Coma After Cardiac Arrest in the Era of Therapeutic Hypothermia.
De Georgia, Michael, Raad, Bassel

CONTINUUM: Lifelong Learning in Neurology. 18(3) Critical Care Neurology 515-531, June 2012.
DOI: 10.1212/01.CON.0000415425.68900.c6

100

Myoclonus

- Myoclonus Status Epilepticus at 24 hrs → poor outcomes (FPR 0%)
- Presence of myoclonus pts with TTM may have good outcomes (FPR 5 [3–8] %; sensitivity 33%)
- Some TTM patients may display brief myoclonic jerks or tonic-clonic activity after rewarming and d/c of sedation and paralytic agents.

C. Sandroni et al. / Resuscitation 85 (2014) 1779–1789

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Myoclonus Status Epilepticus

- continuous andgeneralised myoclonus persisting for ≥30 min
- Using the presence of a status myoclonus within 48 h from ROSC in combination with other predictors to predict poor outcome in comatose survivors of cardiac arrest, either TTM or non-TTM

C. Sandroni et al. / Resuscitation 85 (2014) 1779–1789

103

Neurophysiologic studies

EEGs and SSEPs

109

112

Cerebral Function Monitoring

Amplitude-Integrated EEG – aEEG

113

aEEG

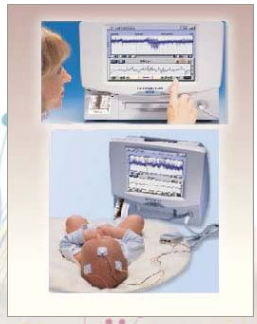
- Displays minimum and maximum amplitude of all background activities over a preset time interval (generally 1-2 secs)
- Provides a good measure of background activity; hence it is also known as Cerebral Function Monitor (CFM)

114

What is CFM

- Single EEG Lead (3 wires)
- Bi-parietal or bi-temporal
- Monitor Global Electrocortical Activity
- Special Filtering
- Compression
- Very Slow, Trend Display

115



116

Single EEG Lead

- 3 Electrodes
  - 2 Active
  - 1 Noise Suppression
- Bi-parietal placement with Needles or Disks
- Bi-Temporal (forehead) with Hydrogel

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Global Electrocortical Activity

- Limited number of electrodes
- Global activity only
- Will not localize lesion
- May not see focal seizures
- High level = high activity
- Low level = suppression

118

Normal CFM

- Sleep/Wake Cycling
- Upper Margin > 10 µvolts
- Lower Margin > 5 µvolts
- Limited Variability

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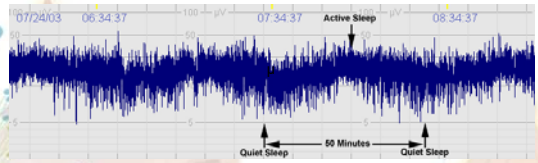
Sleep/Wake Cycling



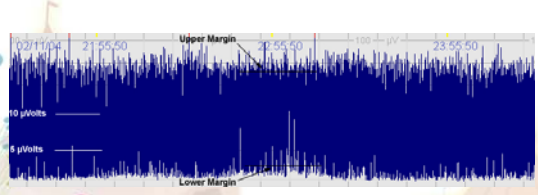
120

Moderately Abnormal

- No Sleep/Wake
- Upper Margin > 10 µVolts
- Lower Margin < 5 µVolts
- Increased variability

121

Moderately Abnormal



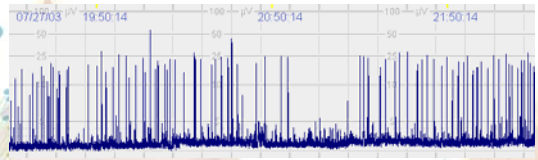
122

Severely Abnormal

- No Sleep/Wake
- Upper Margin < 10 μVolts
- Greatly reduced variability

123

Severely Abnormal



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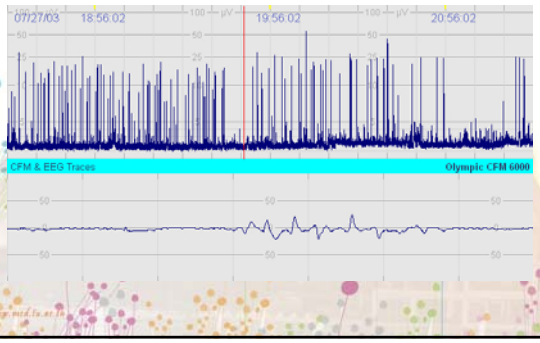
Burst Suppression



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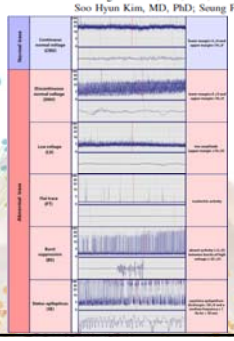
Continuous Amplitude-Integrated Electroencephalographic Monitoring Is a Useful Prognostic Tool for Hypothermia-Treated Cardiac Arrest Patients

Sang Hoon Oh, MD; Kyu Nam Park, MD, PhD; Young-Min Shon, MD, PhD; Young-Min Kim, MD, PhD; Han Joon Kim, MD, PhD; Chun Song Youn, MD; Soo Hyun Kim, MD, PhD; Seung Pill Choi, MD, PhD; Seok Chan Kim, MD, PhD



The time to normal trace (TTNT) <24 hours was associated with good neurological outcome

Circulation. 2015;132:1094-1103

126

EEGs

- predictive of poor outcome
- diagnose seizures and status epilepticus
- differentiate seizures from myoclonus and shivering

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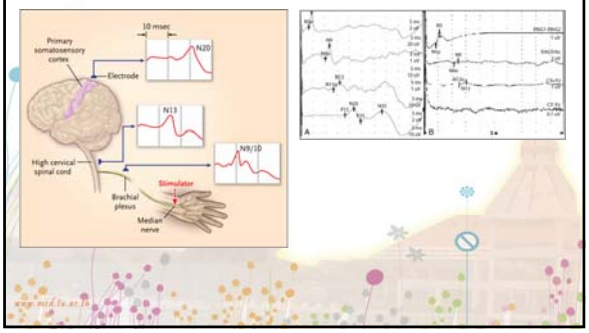
Predictive value of EEGs

- malignant EEG patterns → poor outcomes (FPR 3%)
- Some pts with malignant EEG patterns after TH may have good outcomes
- EEG severity grading during both TH and NT statistically correlated with outcome (grade 1 = good, grade 3 = poor).
- Other EEG features correlating with poor outcome included seizures, nonreactive background, and epileptiform discharges.

128

Somatosensory-Evoked Potentials



129

SSEPs

- bilateral absence of N20 responses recorded 1 to 3 days after cardiac arrest → poor outcomes
- Some pts after TH with absence of N20 responses reported good outcomes

130

BIOCHEMICAL MARKERS OF CEREBRAL INJURY

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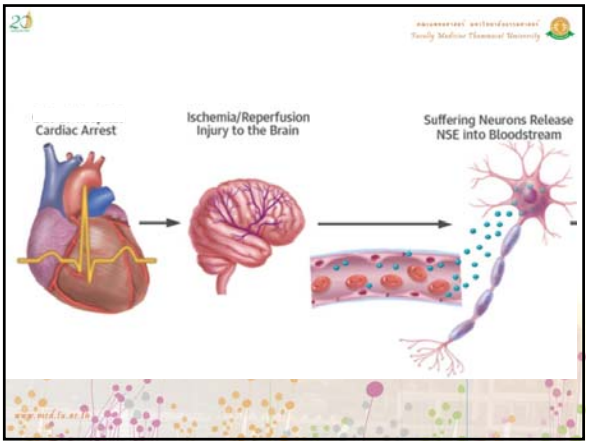

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Serum Neuron Specific Enolase (NSE)

- NSE level > 33 µg/L at 24, 48, or 72 hrs after arrest → poor outcome (FPR 0%)
- In pts with TTM → NSE level > 33 µg/L may have good outcomes (FPR 22 – 29%)

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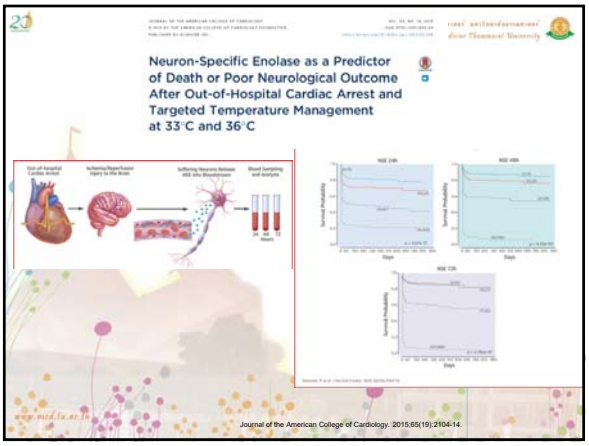

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Assessment of Procalcitonin to Predict Outcome in Hypothermia-Treated Patients after Cardiac Arrest

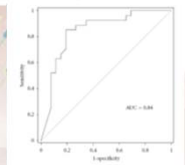
Pascal Stammet,1 Yvan Devaux,2 Francisco Azuaje,2 ChristopheWerer, Christiane Lorang,1 Georges Gilson,3 andMartinMax1 , 2011

TABLE 2: Biological parameters at 48 h after CA.

	Good outcome (n = 27)	Bad outcome (n = 26)	P
PCT (ng/mL)	0.27 (0–0.72)	3.7 (0.84–33.63)	<0.001
CRP (mg/L)	94 (79–157)	139 (105–175)	0.12
WBC (cells/mm³)	9530 (7235–12935)	12460 (9450–17550)	0.18

PCT procalcitonin; CRP C-reactive protein; WBC white blood cell count.

แสดงว่า PCT สามารถเป็นตัววัดที่แยก Good and Bad outcome ได้



A receiver operating characteristic curve (ROC) analysis revealed a capacity of PCT to predict neurological outcome with an AUC of 0.84 (95% CI 0.73–0.96; **P < 0.0001**)

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NEUROIMAGING

CT or MRI

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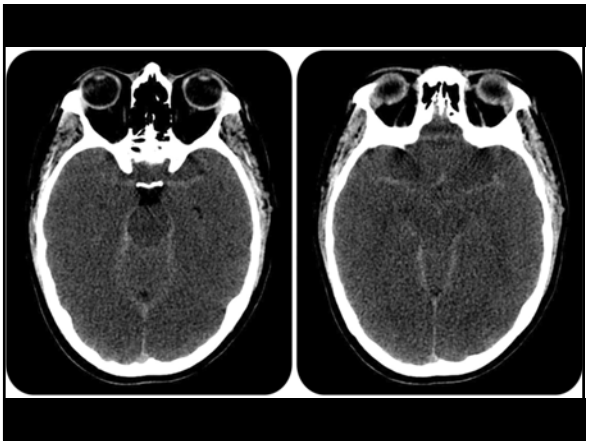

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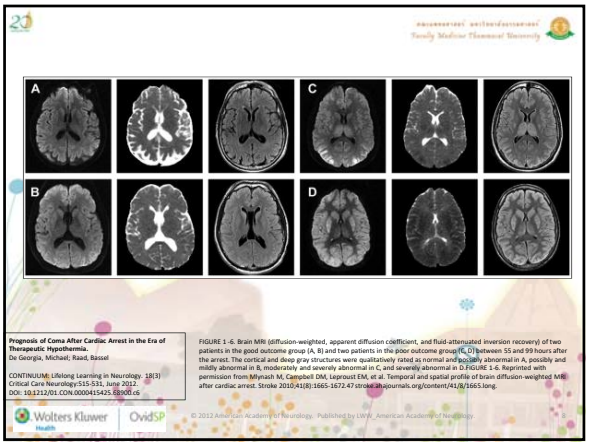

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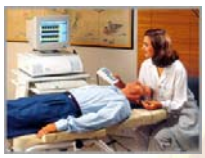
Transcranial Doppler (TCD)



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Cerebral Circulatory Arrest

- Systolic spikes or oscillating flow
- Absent flow
  - ? Transmission difficulty
- Confirmation with extra- and intra-cranial doppler, bilaterally on 2 exams 30 min apart
- Disappearance of intracranial flow signals together with typical extracranial signs can be accepted

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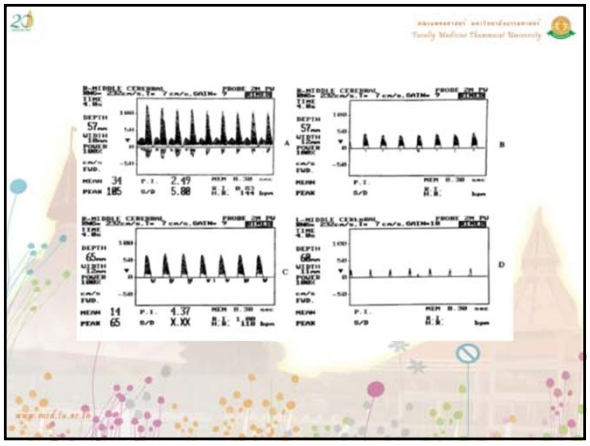

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HRV for 16 cases

Mann-Whitney U Test Survival (n=8) VS Non Survival (n=8)

Initial cooling down | During 33ºc | Rewarm at 37ºc

Wilcoxon signed-rank test

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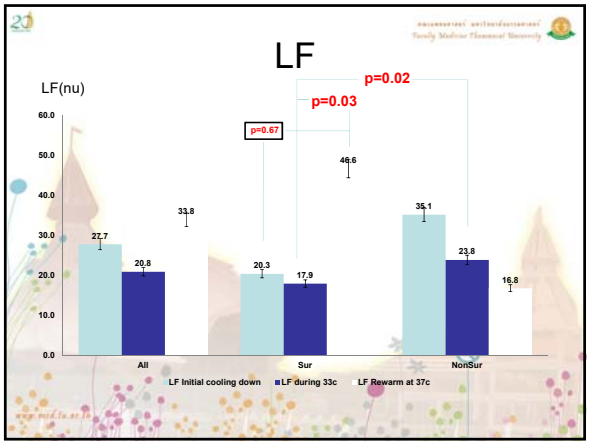
LF



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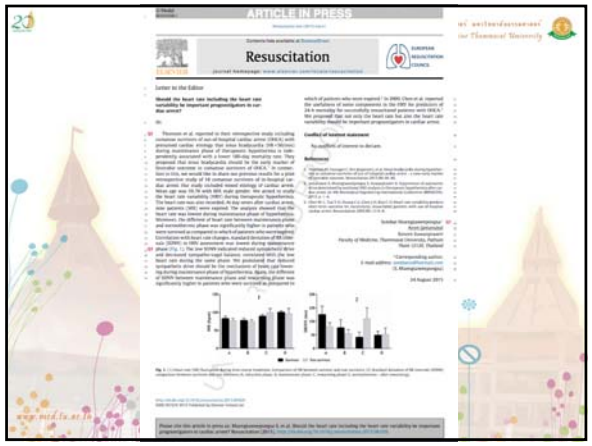

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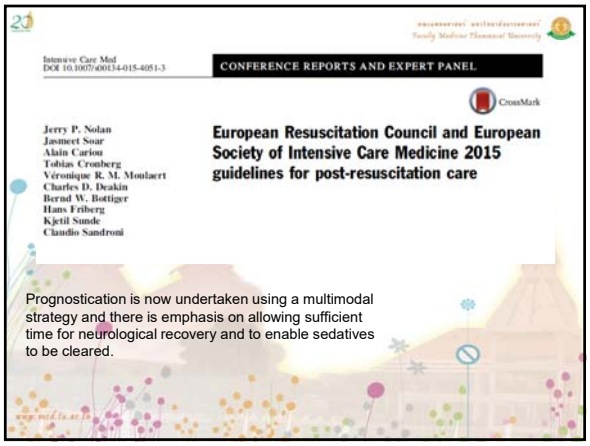

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Part 8: Post–Cardiac Arrest Care

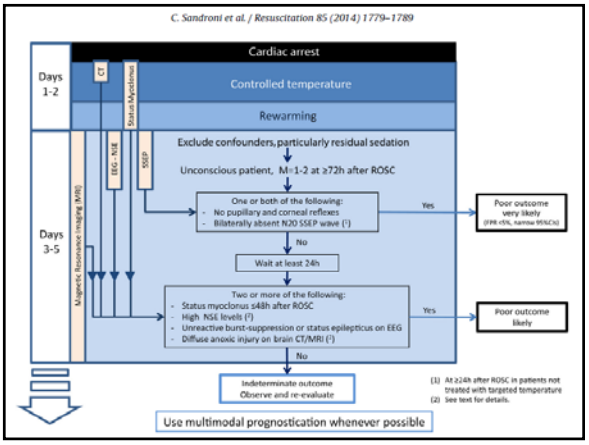
2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Clifton W. Callaway, Chair; Michael W. Donnino; Ericka L. Fink; Romergryko G. Geocadin; Eyal Golan; Karl B. Kern; Marion Leary; William J. Meurer; Mary Ann Peberdy; Trevonne M. Thompson; Janice L. Zimmerman

The earliest time for prognostication using clinical examination in patients treated with TTM, where sedation or paralysis could be a confounder, may be 72 hours after return to normothermia

This approach minimizes the possibility of obtaining false-positive results (ie, inaccurately suggesting a poor outcome)

167



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Summary

- Multimodal prognostication
  - Neurological examination
  - Neuroelectrophysiologic tests
  - Biomarkers
  - Neuroimaging
  - Others
- When uncertainty → FU

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