
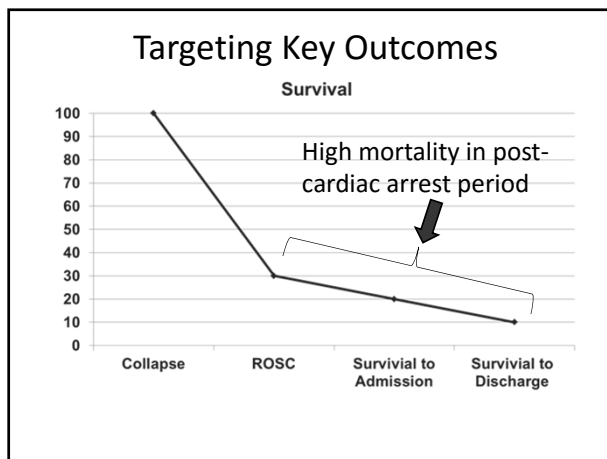


Post-cardiac Arrest Care: TTM and Prognostication

2015 ACLS Update Course

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Chain of Survival in 2010

Chain of survival

成人生命之鏈



儘早辨識及啟動
緊急醫療網



儘早CPR



儘快電擊



有效的ALS



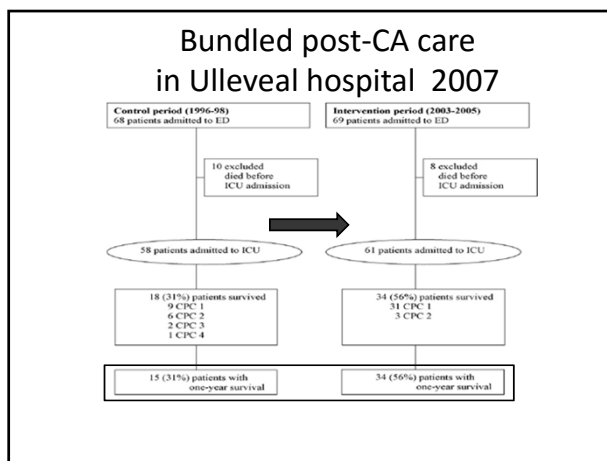
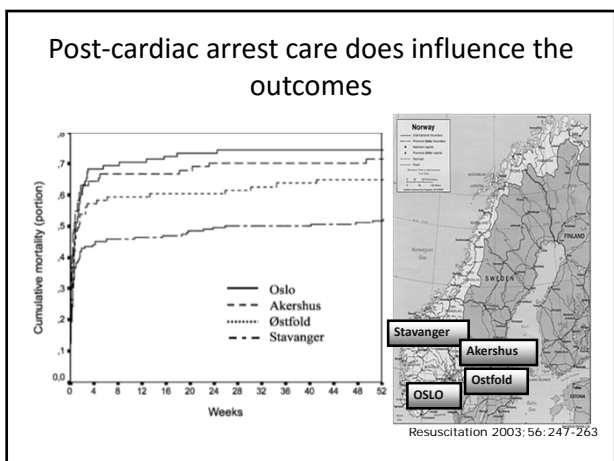
整合性復甦
後照護

What happened after “successful” resuscitation

~~Live Happily Ever After~~

- 72% died in the hospital in Ontario (Canada)
- 75% died in the hospital in Taipei (Taiwan)
- 68% died within 30 days in Goteborg (Sweden)
- 65% died within 30 days in Rochester (USA)

The majority of cardiac arrest patients die after successful resuscitation



Guideline for post-CA care

- ILCOR examined topics and then generated a prioritized list of questions for systematic review.
- Questions were first formulated in PICO (population, intervention, comparator, outcome) format
- contains modifications of the Class III recommendation and introduces LOE B-R (randomized studies) and B-NR (nonrandomized studies) as well as LOE C-LD (limited data) and LOE C-EO (consensus of expert opinion).

Post-Resuscitation Status

- Hypovolemic shock
- Cardiogenic shock
- Vasodilatory shock associated with the systemic inflammatory response syndrome (SIRS)
 - sepsis like syndrome

A critical component of ACLS

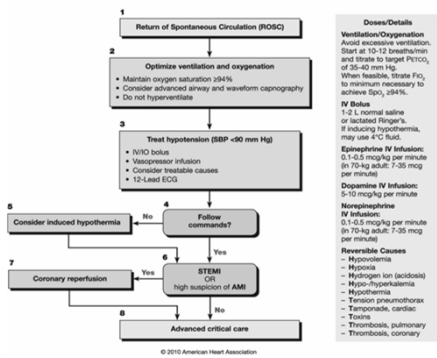
- Most deaths occur during the first 24 hours after cardiac arrest
- Because multiple organ systems are affected after cardiac arrest, successful post-cardiac arrest care will benefit from the development of system-wide plans for proactive treatment of these patients
- Protocolized hemodynamic optimization and multidisciplinary early goal-directed therapy protocols have been introduced as part of a bundle of care to improve survival rather than single interventions

Recommendation Systemic care

- A comprehensive, structured, multidisciplinary system of care should be implemented in a consistent manner for the treatment of post-cardiac arrest patients. (Class I, LOE B) (LAST UPDATED: Oct 2010)
- Include : therapeutic hypothermia, optimization of hemodynamics and gas exchange, immediate coronary reperfusion when indicated, glycemic control and neurological diagnosis, management, and prognostication

Post-cardiac arrest care

Adult Immediate Post-Cardiac Arrest Care



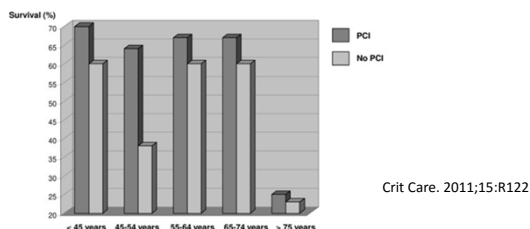
Cardiovascular Care - Updated

- a coronary artery lesion amenable to emergency treatment was found in 96% of patients with ST elevation and in 58% of patients without ST elevation.

PROCAT (Parisian Region Out of hospital Cardiac Arrest) registry. Circ Cardiovasc Interv. 2010;3:200-207. doi: 10.1161/CIRCINTERVENTIONS.109.913665.

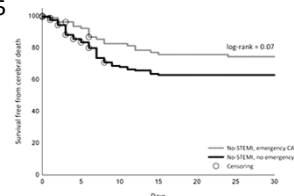
Recommendation for CV care -1

- A 12-lead ECG should be obtained as soon as possible after ROSC to determine whether acute ST elevation is present. (Class I, LOE B)



Emergent Coronary Angiography

- Coronary angiography should be performed emergently (rather than later in the hospital stay or not at all) for OHCA patients with suspected cardiac etiology of arrest and ST elevation on ECG. (Class I, LOE B-NR) NEW: Oct 2015



Recommendation for CV care -2

- Emergency coronary angiography is reasonable for select (eg, electrically or hemodynamically unstable) adult patients who are comatose after OHCA of suspected cardiac origin but without ST elevation on ECG. (Class IIa, LOE B-NR) NEW: Oct 2015
- Coronary angiography is reasonable in post-cardiac arrest patients for whom coronary angiography is indicated regardless of whether the patient is comatose or awake. (Class IIa, LOE C-LD) NEW: Oct 2015

Hemodynamic Goals - Updated

- Hemodynamically unstable can occur for multiple reasons including the underlying etiology of the arrest as well as the ischemia-reperfusion injury from the arrest.
- Avoiding and immediately correcting hypotension (systolic BP < 90 mmHg, MAP < 65 mmHg) during postresuscitation care may be reasonable. (Class IIb, LOE C-LD) NEW: Oct 2015

Identifying an optimal goal

- An optimal goal for the overall patient population may be complicated by individual patient variability.
- The true optimal BP would be that which allows for optimal organ and brain perfusion
- Targets for other hemodynamic or perfusion measures (such as cardiac output, mixed/central venous oxygen saturation, and urine output) remain undefined in post-cardiac arrest patients

Vasopressors

- Vasoactive drugs may be administered after ROSC to support cardiac output, especially blood flow to the heart and brain.
- Unfortunately many adrenergic drugs are not selective and may increase or decrease heart rate and afterload, increase cardiac arrhythmias, and increase myocardial ischemia
- Specific drug infusion rates cannot be recommended because of variations in pharmacokinetics and pharmacodynamics in critically ill patients

Temperature Management After Cardiac Arrest - ILCOR Advisory Statement

3 key questions:

- (1) Should mild induced hypothermia (or some form of targeted temperature management) be used in comatose post-cardiac arrest patients?
- (2) If used, what is the ideal timing of the intervention?
- (3) If used, what is the ideal duration of the intervention?

Circulation. 2015 Oct 4. [Epub ahead of print]

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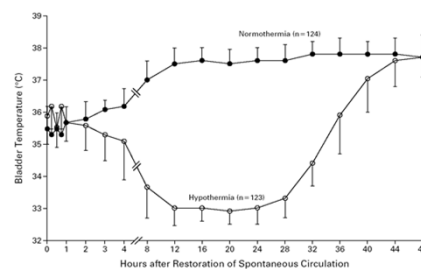
Therapeutic Hypothermia Improves Neurological Functions in Comatose OHCA Survivors – Australia study

Hypothermia : 33°C for 12 hrs after ROSC

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

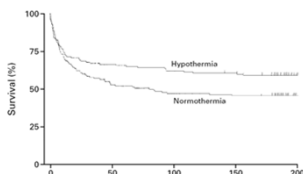
Bernard SA, et al. *N Engl J Med* 2002;346:557-63

Mild Therapeutic Hypothermia to improve the Neurological Outcome after Cardiac Arrest – HACA study



The hypothermia after cardiac arrest study group. *N Engl J Med* 2002;346:549-56

Mild Therapeutic Hypothermia to improve the Neurological Outcome after Cardiac Arrest

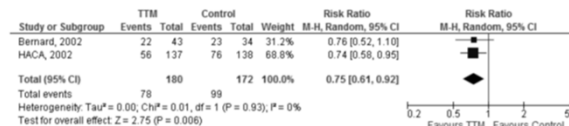


OUTCOME	NORMOTHERMIA no./total no. (%)	HYPOTHERMIA no./total no. (%)	RISK RATIO (95% CI)*	P VALUE†
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02

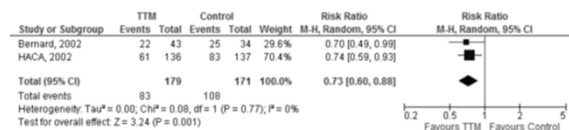
The hypothermia after cardiac arrest study group. *N Engl J Med* 2002;346:549-56

Does TTM help for cardiac arrest?

A. Forest Plot – Outcome: Mortality



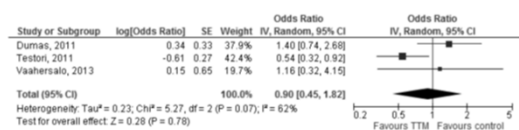
B. Forest Plot – Outcome: Poor Neurologic/Functional Outcome



ILCOR Advisory Statement. Circulation 2015. doi: 10.1161/CIR.0000000000000313

Does TTM help for cardiac arrest? For non-shockable rhythm

C. Forest Plot – Nonshockable rhythm. Outcome: Poor Neurologic Outcome*



ILCOR Advisory Statement. Circulation 2015. doi: 10.1161/CIR.0000000000000933

DOI: 10.1161/CIRCULATIONAHA.115.016317

32°-34° C vs. no hypothermia treatment

The Utility of Therapeutic Hypothermia for Post-Cardiac Arrest Syndrome Patients With an Initial Non-Shockable Rhythm

Running title: *Perman et al., Therapeutic Hypothermia for non-shockable rhythms*

Sarah M. Perman, MD, MSCE¹; Anne V. Grossestreuer, MS^{2,3,4}; Douglas J. Wiebe, PhD^{2,4};
Brendan G. Carr, MD, MSHP⁵; Benjamin S. Abella, MD, MPhil^{3,4}; David F. Gaieski, MD⁵

Mean age was 63±17 years; 51% were male; and 60% had an initial rhythm of PEA. Survival to hospital discharge was greater in TH (17.6% vs. 28.9%; p<0.01), as was discharge CPC of 1-2 (13.7% vs 21.4%; p=0.04).

More Chances of Survival to Discharge for OHCA & IHCA under TTM

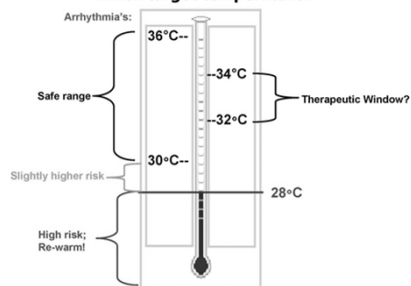
Table 3. Outcomes for the multivariate analysis of the propensity-matched cohort of patients treated with and without therapeutic hypothermia.

Status at Hospital Discharge	Adjusted Odds Ratio ^a
Survival	
Total cohort	2.8 (95% CI: 1.6-4.7)
IHCA	2.2 (95% CI: 0.8-6.2)
OHCA	3.1 (95% CI: 1.6-5.8)
Neurologic Recovery^b	
Total cohort	3.5 (95% CI: 1.8-6.6)
IHCA	4.2 (95% CI 1.2-14.9)
OHCA	2.1 (95% CI 1.0-4.4)

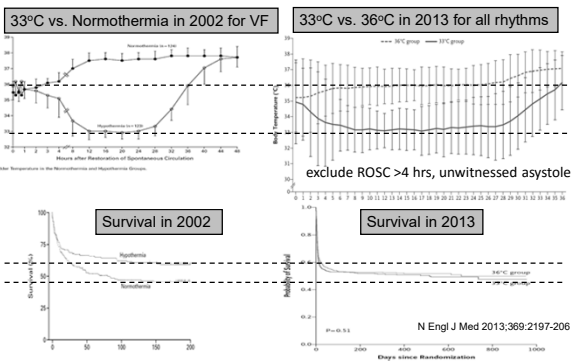
^aCPC 1 or 2; ^b variables included in multivariable model include age, sex, witnessed arrest, initial rhythm (PEA/Asystole), and duration of arrest.

How cool is optimal or adequate

Which target temperature?



Targeted Temperature Management



TTM – Neurological outcomes

OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
HACA study in 2002				
	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

Outcome	33°C Group	36°C Group	Hazard Ratio or Risk Ratio (95% CI) ^a	P Value
TTM study in 2013				
	no./total no. (%)			
Primary outcome: deaths at end of trial	235/473 (50)	225/466 (48)	1.06 (0.89–1.28)	0.51
Secondary outcomes				
Neurologic function at follow-up‡				
CPC of 3–5	251/469 (54)	242/464 (52)	1.02 (0.88–1.16)	0.78
Modified Rankin scale score of 4–6	245/469 (52)	239/464 (52)	1.01 (0.89–1.14)	0.87
Deaths at 180 days	226/473 (48)	220/466 (47)	1.01 (0.87–1.15)	0.92

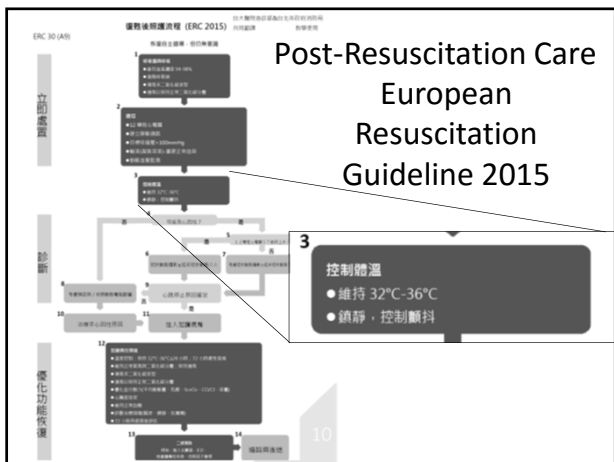
N Engl J Med 2013;369:2197-206

2015 AHA Recommendations—Updated

- We recommend that comatose (ie, lack of meaningful response to verbal commands) adult patients with ROSC after cardiac arrest have TTM
 - Class I**, for VF/pVT OHCA (LOE B-R)
 - Class I**, for non-VF/pVT (non-shockable) and in-hospital cardiac arrest (LOE C-EO)
- We recommend selecting and maintaining a constant temperature between 32°C and 36°C during TTM (Class I, LOE B-R).

Stronger recommendations for TTM for non-shockable rhythms & IHCA

- Stronger than those made in 2015 by ILCOR and are stronger than the recommendations in the 2010 Guidelines.
- The writing group felt that the option for TTM at 36°C diminished theoretical concerns about side effects of TTM for these populations.
- In addition, the writing group was influenced by the high rate of neurologic morbidity in historical cohorts that did not use TTM.



Temperature Management After Cardiac Arrest - ILCOR Advisory Statement

3 key questions:

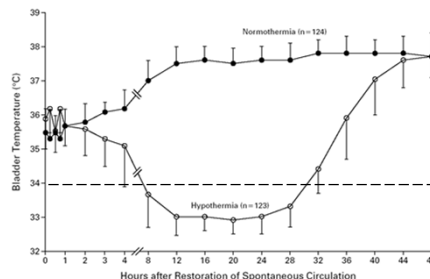
- (1) Should mild induced hypothermia (or some form of targeted temperature management) be used in comatose post-cardiac arrest patients?
- (2) If used, what is the ideal timing of the intervention?
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Circulation. 2015 Oct 4. [Epub ahead of print]

When to Cool

- In HACA study, the median interval between the ROSC and the initiation of cooling was 105 minutes (interquartile range, 61 to 192)
- In Australia study, the core temperature decreased from 34.9°C 30 minutes after ROSC, to 33.5°C 120 minutes after ROSC

Mild Therapeutic Hypothermia to improve the Neurological Outcome after Cardiac Arrest



Bladder Temperature in the Normothermia and Hypothermia Groups. The hypothermia after cardiac arrest study group. *N Engl J Med* 2002;346:549-56

Time Windows of Initiating Hypothermia

- Rapid initiation of hypothermia, but at a maximum within six hours of ROSC.
 - ~Massachusetts General Hospital
- Less than 12 hours since ROSC.
 - ~Hospital of the University of Pennsylvania
- Exclude cases greater than 6 hours post arrest
 - ~University of Illinois Medical Center, Chicago
- >4 hours (240 minutes) from ROSC to screening
 - ~TTM trial 2013

Cooling just after ROSC

Induction of Therapeutic Hypothermia by Paramedics After Resuscitation From VF OHCA - A Randomized Controlled Trial

- OHCA with an initial rhythm of VF
- Pre-hospital cooling with a rapid infusion of 2 L of ice-cold lactated Ringer's solution (n=118) vs. cooling after hospital admission (n=116).
- Patients allocated to paramedic cooling received a median of 1900 mL of ice-cold fluid.
- This resulted in a mean decrease in core temperature of 0.8°C

Circulation. 2010 Aug 17;122(7):737-42. Bernard, SA, et al. Circulation. 2010;122:737-742

Primary Outcome

- Functional status at hospital discharge, with a favorable outcome defined as discharge either to home or to a rehabilitation facility.

	Paramedic Cooling (n=118)	Hospital Cooling (n=116)	P*
Favorable outcome, n (%; 95% CI)	56 (47.5; 38.2–56.9)	61 (52.6; 43.1–61.9)	0.433
Discharge to home, n (%; 95% CI)	24 (20.3; 13.5–28.7)	34 (29.3; 21.2–38.5)	...
Discharge to rehabilitation, n (%; 95% CI)	32 (27.1; 19.3–36.1)	27 (23.3; 15.9–32.0)	...
Discharge to nursing home awake, n	0	0	...
Discharge to nursing home comatose, n (%; 95% CI)	0	1 (0.9; 0.02–4.7)	...
Dead, n (%; 95% CI)	62 (52.5; 43.1–61.8)	54 (46.6; 27.2–56.0)	...

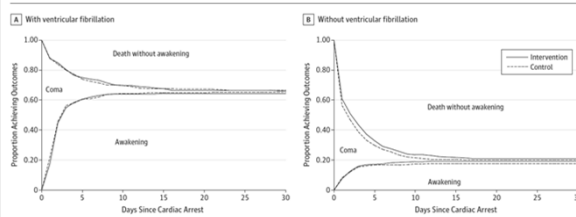
Bernard, SA, et al. Circulation. 2010;122:737-742

Effect of Prehospital Induction of Mild Hypothermia on Survival and Neurological Status Among Adults With Cardiac Arrest

JAMA. 2014;311(1):45-52

Francis Kim, MD, Graham Nichol, MD, MPH, Charles Maynard, PhD, Al Hallstrom, PhD, Peter J Kudenchuk, MD, Thomas Rex, MD, MPH, Michael K. Copass, MD, David Carlbom, MD, Steven Deem, MD, W. T. Longstreth Jr, MD, Michele Olsufka, RN, Leonard A. Cobb, MD

Figure 2. The Proportion of Comatose Patients Achieving Either Death Without Awakening or Awakening as a Function of Days After Cardiac Arrest for Enrolled Patients



Intra-Arrest Transnasal Evaporative Cooling – PRINCE study

Table 1. Baseline Characteristics

	Treatment (n=93)
Age, y, mean	66.1
Male sex, n (%)	67 (72.0)
Bystander CPR, n (%)	33 (35.5)
Cardiac cause, n (%)	78/90 (86.7)
VF, n (%)	27 (29.0)
PEA, n (%)	19 (20.4)
Asystole, n (%)	47 (50.5)

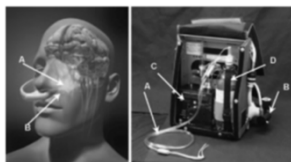
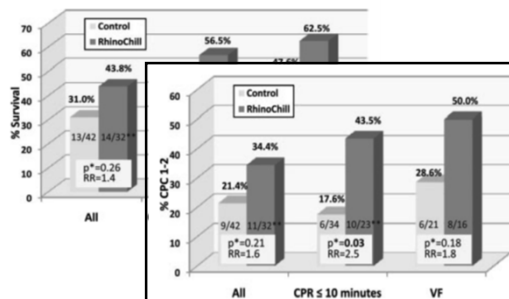


Figure 1. RhinoChill cooling device.

Castreñon M, Nordberg, et al. Circulation. 2010;122:729-736

Outcome in Intra-Arrest Cooling



Castreñon M, Nordberg, et al. Circulation. 2010;122:729-736

2015 AHA Recommendation—New Pre-hospital cooling

- We recommend against the routine pre-hospital cooling of patients after ROSC with rapid infusion of cold intravenous fluids (Class III: No Benefit, LOE A).
- Whether different methods or devices for temperature control outside of the hospital are beneficial is unknown.

Temperature Management After Cardiac Arrest - ILCOR Advisory Statement

3 key questions:

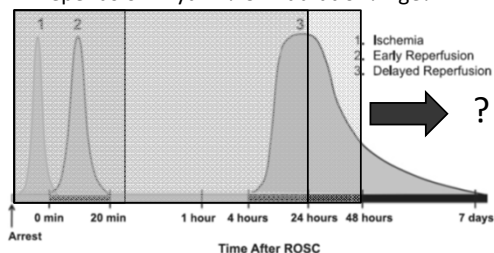
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Circulation. 2015 Oct 4. [Epub ahead of print]

How long ?

Different “dosage” for different patients?

Depends on rhythm? CPR duration? Age?.....



Time course of neuron damage after cardiac arrest

CHEST 2014; 145(2):386–393

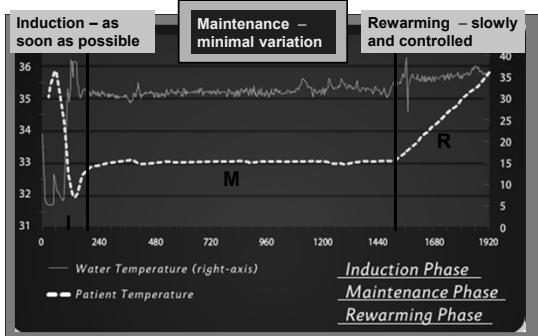
Ideal duration of TTM

- There are no data that can be used to compare different durations of targeted temperature management in humans.

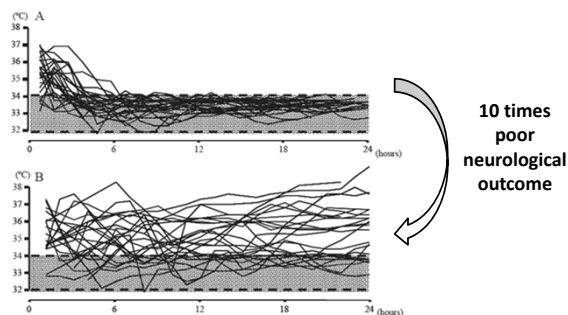
Recommendation

- We suggest that if targeted temperature management is used, duration should be at least 24 hours as done in the 2 largest previous RCTs - *HACA in 2002 & TTM in 2013* (weak recommendation, very low-quality evidence).

Three Phases in Hypothermia



Good temperature control is the crucial



Am J Emerg Med. 2012 Nov;30(9):1838-44

2015 AHA Recommendations—Updated

- We recommend that comatose (ie, lack of meaningful response to verbal commands) adult patients with ROSC after cardiac arrest have TTM
 - Class I**, for VF/pVT OHCA (LOE B-R)
 - Class I**, for non-VF/pVT (non-shockable) and in-hospital cardiac arrest (LOE C-EO)
- We recommend selecting and maintaining a constant temperature between 32°C and 36°C during TTM (Class I, LOE B-R).

Fever prevention

- It may be reasonable to actively prevent fever in comatose patients after TTM. (Class IIb, LOE C-LD) NEW: Oct 2015

Seizure Management - Updated

- The prevalence of seizures, nonconvulsive status epilepticus among patients who are comatose after CA is estimated to be 12% to 22%
- Not support prophylactic administration of anticonvulsant drugs
- An EEG for the diagnosis of seizure should be promptly performed and interpreted, and then should be monitored frequently or continuously in comatose patients after ROSC. (Class I, LOE C-LD) NEW updated 2015
- The same anticonvulsant regimens for the treatment of status epilepticus caused by other etiologies may be considered after cardiac arrest. (Class IIb, LOE C-LD) NEW updated 2015

Respiratory Care – Updated for CO₂

- Higher PaCO₂ may be permissible in patients with acute lung injury or high airway pressures.
- Mild hypocapnia might be useful as a temporizing measure when treating cerebral edema
- Maintaining the PaCO₂ within a normal physiological range, taking into account any temperature correction, may be reasonable. (Class IIb, LOE B-NR) NEW updated Oct 2015

Respiratory Care – Updated for O₂

- To avoid hypoxia in adults with ROSC after cardiac arrest, it is reasonable to use the highest available oxygen concentration until the arterial oxyhemoglobin saturation or the partial pressure of arterial oxygen can be measured. (Class IIa, LOE C-EO) NEW: Oct 2015
- When resources are available to titrate the FiO₂ and to monitor oxyhemoglobin saturation, it is reasonable to decrease the FiO₂ when oxyhemoglobin saturation is 100%, provided the oxyhemoglobin saturation can be maintained at 94% or greater. (Class IIa, LOE C-LD) NEW updated Oct 2015

Sedation After Cardiac Arrest

- Sedation, analgesia, and occasionally neuromuscular relaxation are routinely used to facilitate induced hypothermia and to control shivering.
- The duration of neuromuscular blocker use should be minimized.
- It is reasonable to consider the titrated use of sedation and analgesia in critically ill patients who require mechanical ventilation or shivering suppression during induced hypothermia after cardiac arrest. (Class IIb, LOE C) LAST UPDATED: Oct 2010

Prognostication of Outcome - Updated

- Focused recommendations on tests : false-positive rates (FPRs) close to 0%, with narrow 95% confidence intervals (0%–10%).
- Delayed conscious recovery can be related to :
 - (1) More slowly metabolized sedatives or neuromuscular blockers in post-cardiac arrest patients,
 - (2) Injured brains may be more sensitive to the depressant effects of various medications

Recommendations for Timing of Neuro-prognostication

- 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 (Class IIb, LOE C-EO).
- Operationally, the timing for prognostication is typically 4.5 to 5 days after ROSC for patients treated with TTM

Recommendations for Neuro-prognostication without TTM

- We recommend the earliest time to prognosticate a poor neurologic outcome using clinical examination in patients not treated with TTM is 72 hours after cardiac arrest (Class I, LOE B-NR).
- This time until prognostication can be even longer than 72 hours after cardiac arrest if the residual effect of sedation or paralysis confounds the clinical examination (Class IIa, LOE C-LD).

Clinical Examination Findings That Predict Poor Outcome

- Bilaterally absent pupillary light reflex at 72 to 108 hours : FPR 1% (95% CI, 0%–3%).
- Bilaterally absent corneal reflexes at 72 to 120 hours : FPR 2% (95% CI, 0%–7%).
- Extensor posturing or no motor response to pain at 36 to 108 hours: FPR 10% (95% CI, 7%–15%)
- Any myoclonus within 72 hours : 5% FPR (95% CI, 3%–8%).
- **Recommendation:** In comatose patients who are treated with TTM, the absence of pupillary reflex to light at 72 hours or more after cardiac arrest is useful to predict poor neurologic outcome (FPR, 1%; 95% CI, 0%–3%; Class I, LOE B-NR).

EEG Findings to Predict Outcome

- In comatose post-cardiac arrest patients who are treated with TTM, it may be reasonable to consider persistent absence of EEG reactivity to external stimuli at 72 hours after cardiac arrest, and persistent burst suppression on EEG after rewarming, to predict a poor outcome (FPR, 0%; 95% CI, 0%–3%; Class IIb, LOE B-NR).
- Intractable and persistent (more than 72 hours) status epilepticus in the absence of EEG reactivity to external stimuli may be reasonable to predict poor outcome (Class IIb, LOE B-NR).

Evoked Potentials to Predict Outcome

- In patients who are comatose after resuscitation from cardiac arrest regardless of treatment with TTM, it is reasonable to consider bilateral absence of the N20 SSEP wave 24 to 72 hours after cardiac arrest or after rewarming a predictor of poor outcome (FPR, 1%; 95% CI, 0%–3%; Class IIa, LOE B-NR).

Imaging Tests to Predict Outcome 2015 Recommendations—New

- In patients who are comatose after resuscitation from cardiac arrest and not treated with TTM, it may be reasonable to use the presence of a marked reduction of the GWR on brain CT obtained within 2 hours after cardiac arrest to predict poor outcome (Class IIb, LOE B-NR).
- It may be reasonable to consider extensive restriction of diffusion on brain MRI at 2 to 6 days after cardiac arrest in combination with other established predictors to predict a poor neurologic outcome (Class IIb, LOE B-NR). - 0% FPR (95% CI, 0%–45%).
- Acquisition and interpretation of imaging studies have not been fully standardized; interobserver variability; the assumption that images are performed in centers with expertise.

Blood Markers to Predict Outcome

- Given the possibility of high FPRs, blood levels of NSE and S-100B should not be used alone to predict a poor neurologic outcome (Class III: Harm, LOE C-LD).
- Laboratory standards for NSE and S-100B measurement vary between centers, making comparison of absolute values difficult.

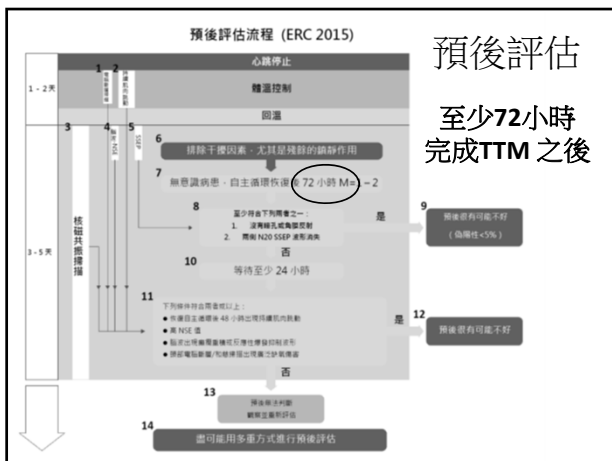
Organ Donation

- Tissue donation (cornea, skin, and bone) is almost always possible if post-cardiac arrest patients die.
- Organs transplanted from cardiac arrest donors also have success rates comparable to similar donors with other conditions.

Organ donation

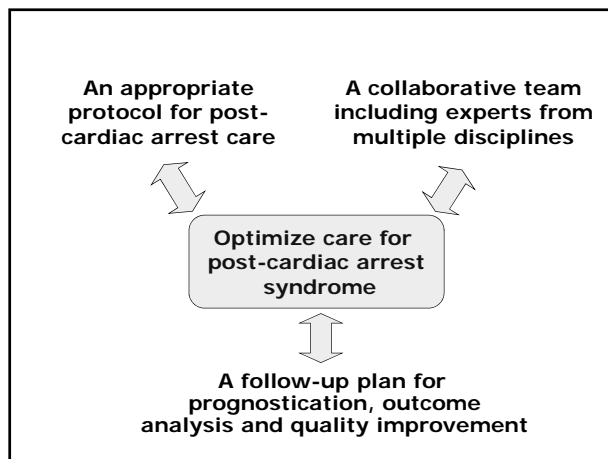
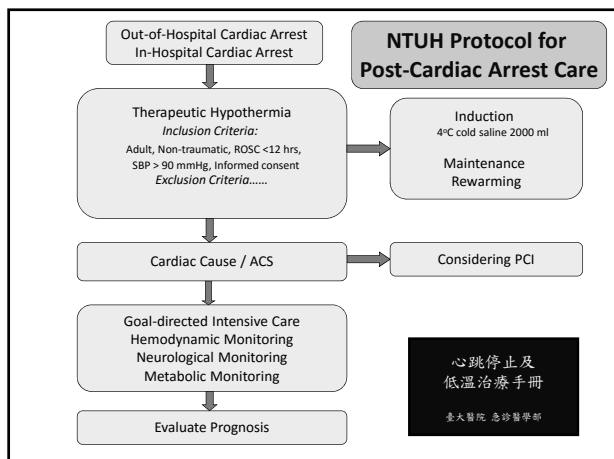
2015 Recommendations

- We recommend that all patients who are resuscitated from cardiac arrest but who subsequently progress to death or brain death be evaluated for organ donation (Class I, LOE B-NR).
- Patients who do not have ROSC and who would otherwise have termination of efforts may be considered candidates for kidney or liver donation in settings where programs exist (Class IIb, LOE B-NR).
- The **ethics and practical aspects** of these programs are quite complex.



TTM for Cardiac Arrest in Taiwan after 2015





Integrate the Bundled post-cardiac arrest care

Start treatment protocol in your hospital