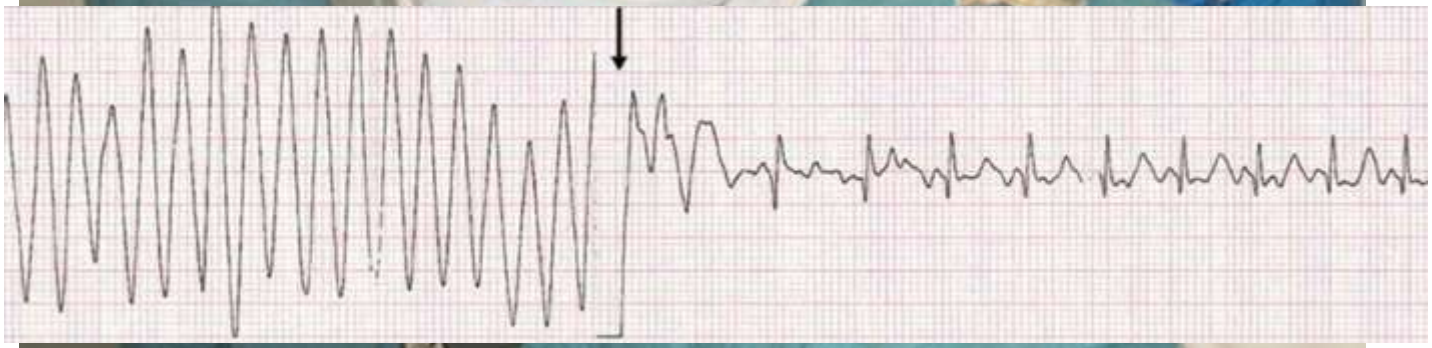
Post-resuscitation care of the cardiac arrest survivor

Dr Ali Ashraf

Intensivist

GUMS porsina H


CODE BLUE!!



Out of Hospital Cardiac Arrest

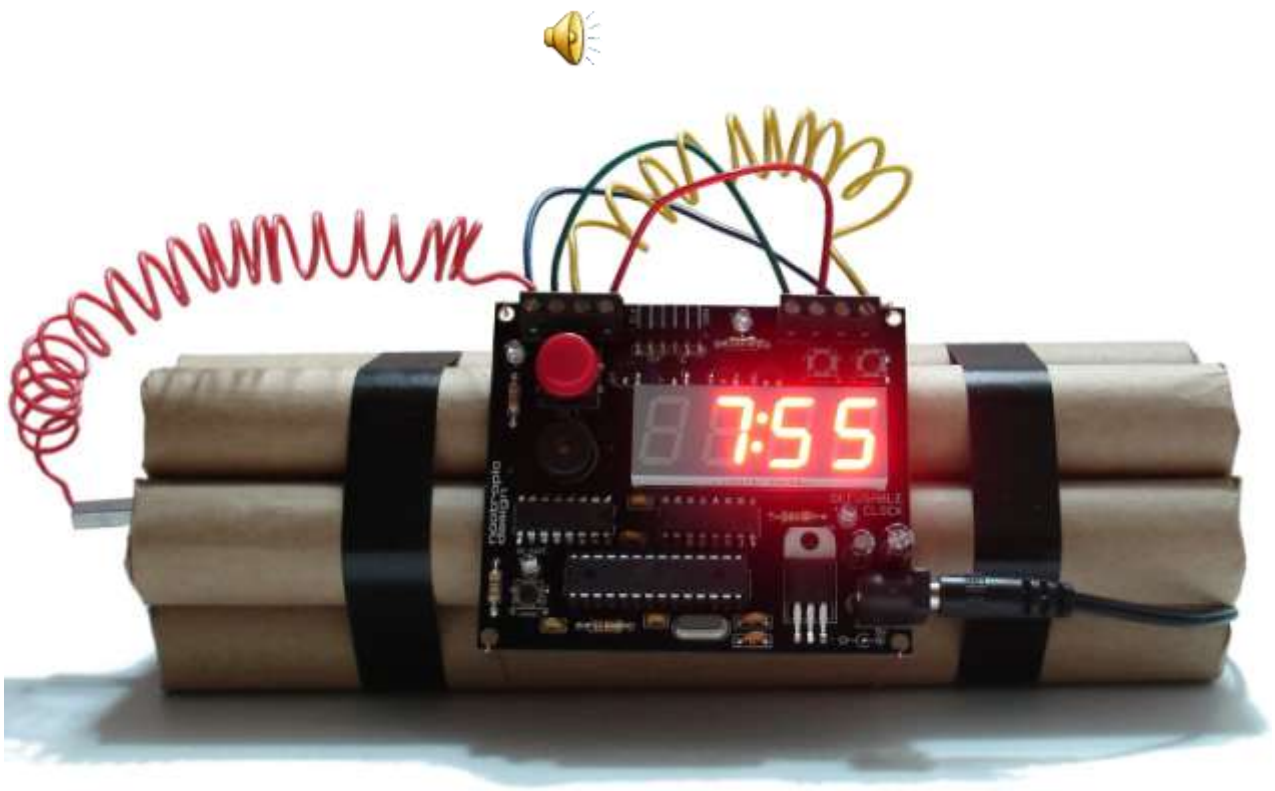
- Cardiac arrest is **common**
  - 295,000 OHCA per year in US
    - 23% VF
    - 31% Bystander CPR
  - Median survival all rhythms 7.9%, VF 21%

Circulation 2010;Jan 26:e12-13

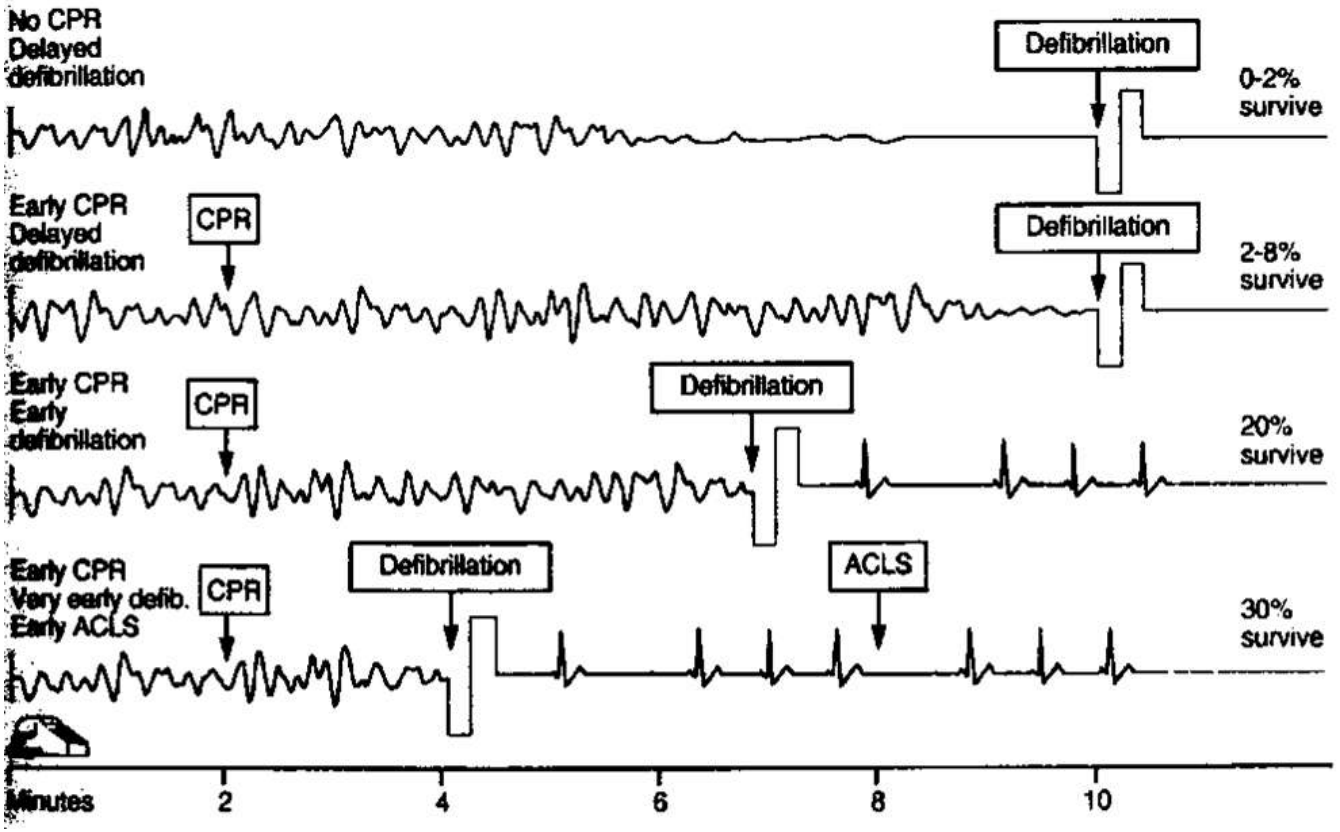
How to Save Lives in Cardiac Arrest

- **Bystander CPR**
  - Chest compressions only
- **Minimally interrupted CPR**
- **Modern post-resuscitation care**
  - Therapeutic hypothermia
  - Cardiac and hemodynamic support

Hands only CPR



How to save life?

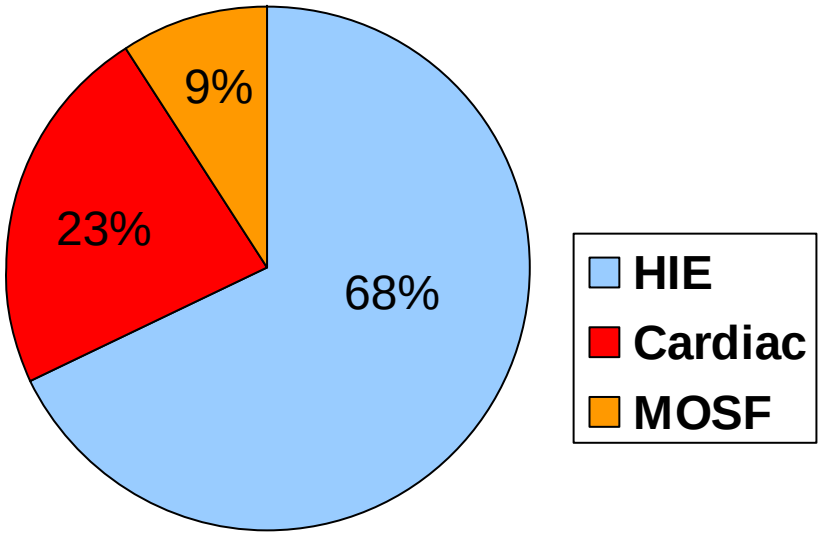


Improving Postresuscitation Outcomes

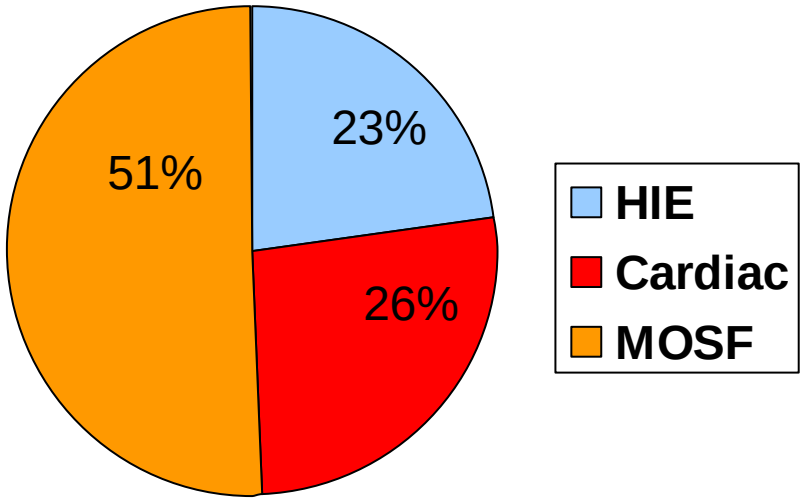
- Postresuscitation care is a critical component
- Patient mortality remains high
- Ultimate prognosis in the first 72 hours may be difficult to determine
- survivors of cardiac arrest have the potential to lead normal lives

From what do they die…?

Cause of Death in OHCA



Cause of death in IHCA

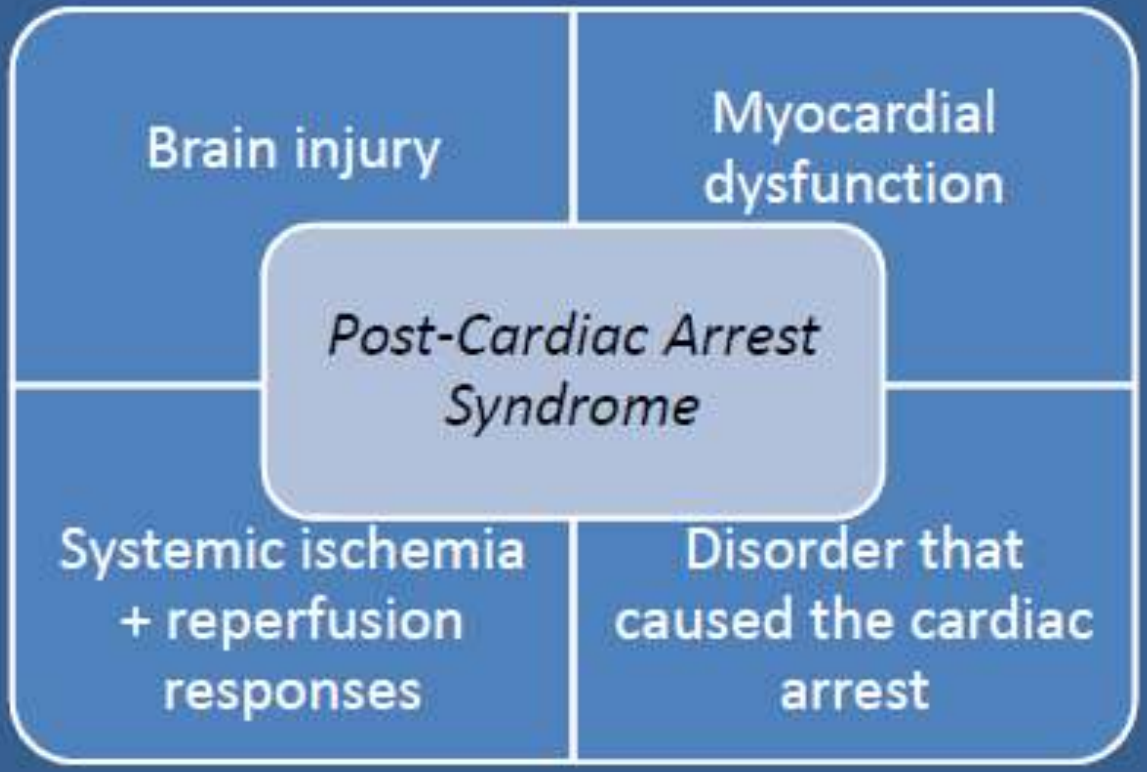


Laver. Intensive Care Med 2004;30:2126

Post-arrest care is as important as intra-arrest care

- Once we've achieved ROSC our job is not over
- maintaining blood pressure
- cerebral perfusion
- adequate sedation,
- cooling and preventing hyperthermia
- Antiarrhythmic medications,
- Oxygen delivery & avoiding hyperoxia
- PCI who need it
- Treating the underlying cause.

Consequences From Cardiac Arrest

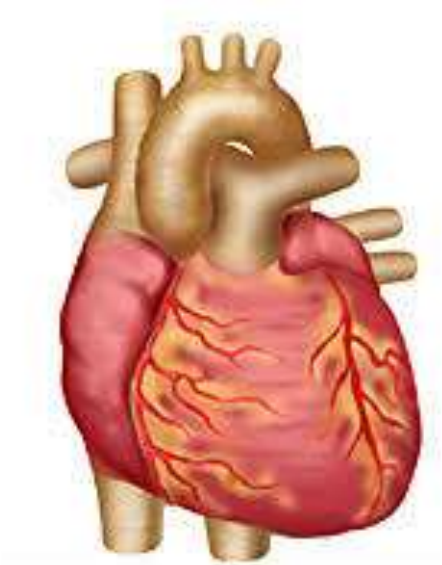


The post-cardiac arrest syndrome

- post-cardiac arrest brain injury

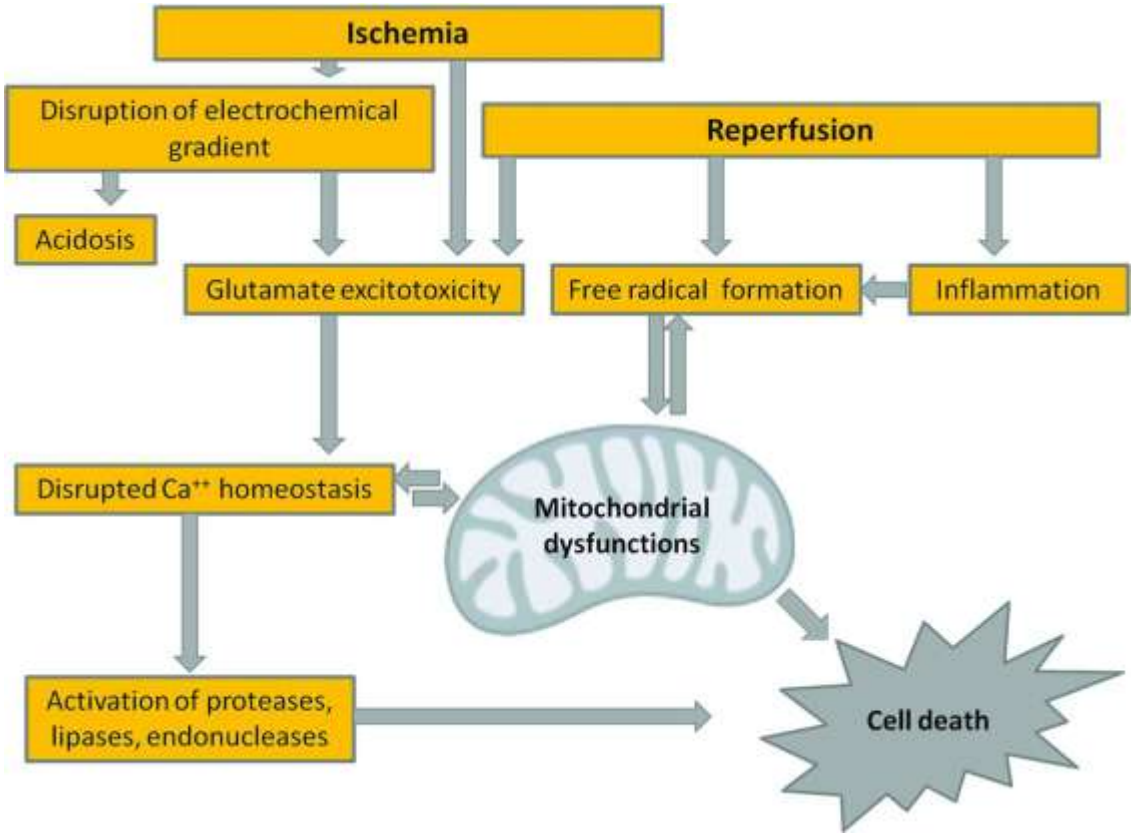
The post-cardiac arrest syndrome

- post-cardiac arrest myocardial dysfunction



The post-cardiac arrest syndrome

- systemic ischaemia/reperfusion response



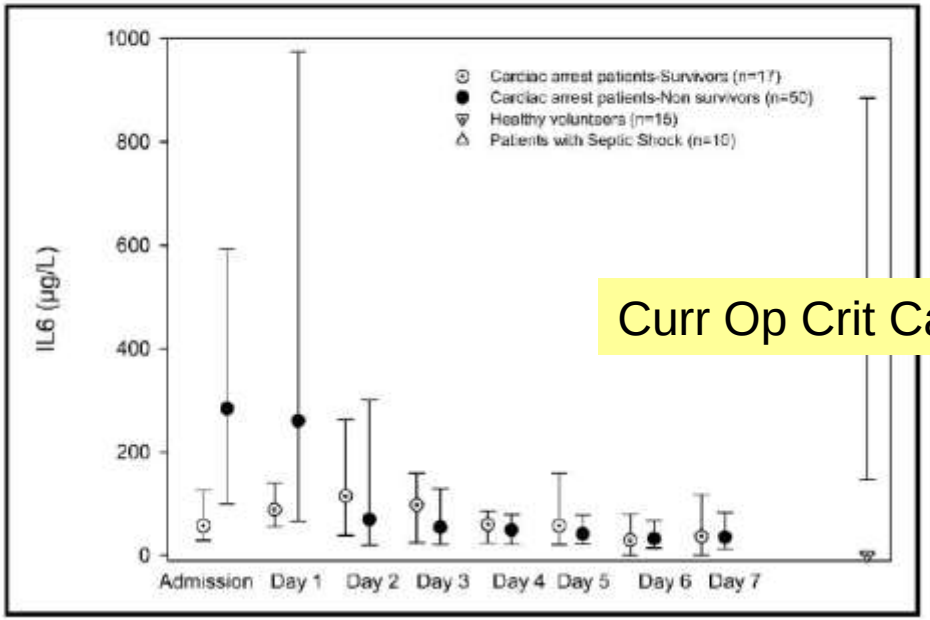
The post-cardiac arrest syndrome

- persistent precipitating pathology

Postresuscitation syndrome

Postresuscitation disease is characterized by high levels of circulating cytokines and adhesion molecules, the presence of plasma endotoxin, and dysregulated leukocyte production of cytokines: a profile similar to that seen in severe sepsis.

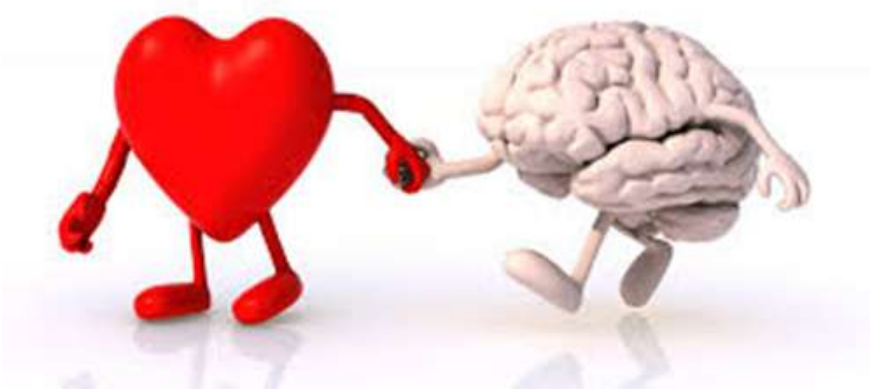
Figure 2. Plasma interleukin-6 (IL-6) kinetics over 7 days in patients who were successfully resuscitated after cardiac arrest



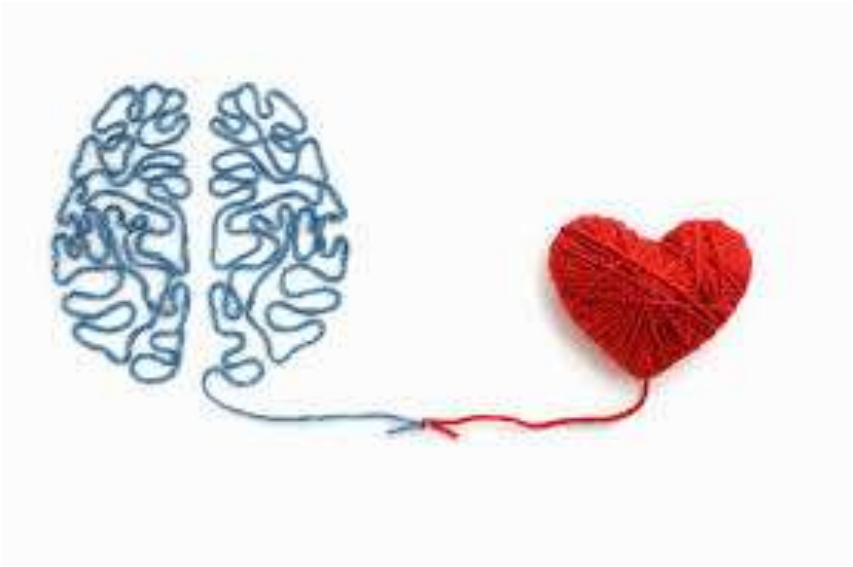
Curr Op Crit Care 2004;10:208-212

Return of Spontaneous Circulation

- The principal objective of postresuscitation care is the re-establishment of effective perfusion of organs and tissue.



Heart and brain protection



Post-arrest care is as important as intra-arrest care

- Once we've achieved ROSC our job is not over
- Good post-arrest care involves maintaining blood pressure
- cerebral perfusion,
- adequate sedation,
- cooling and preventing hyperthermia,
- considering antiarrhythmic medications,
- optimization of tissue oxygen delivery while avoiding hyperoxia, getting patients to PCI who need it,
- looking for and treating the underlying cause.

Myocardial dysfunction after CA

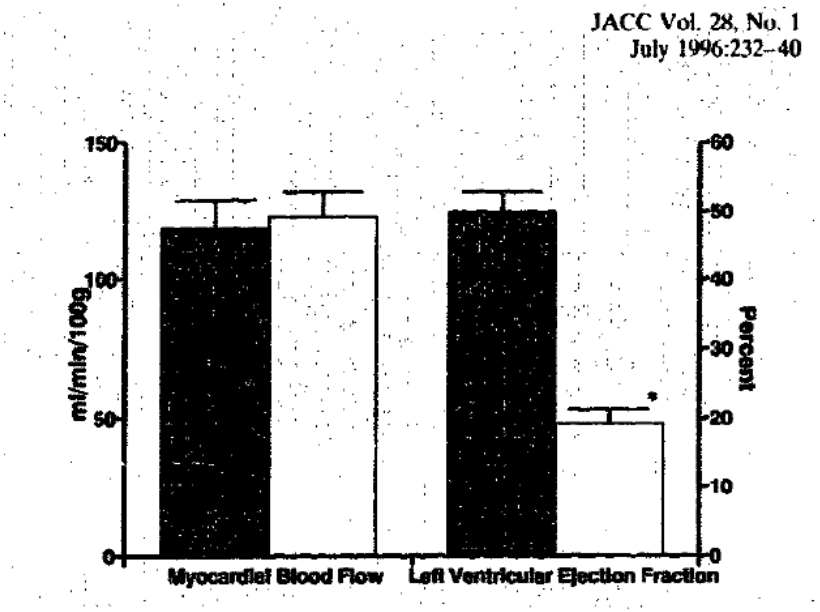
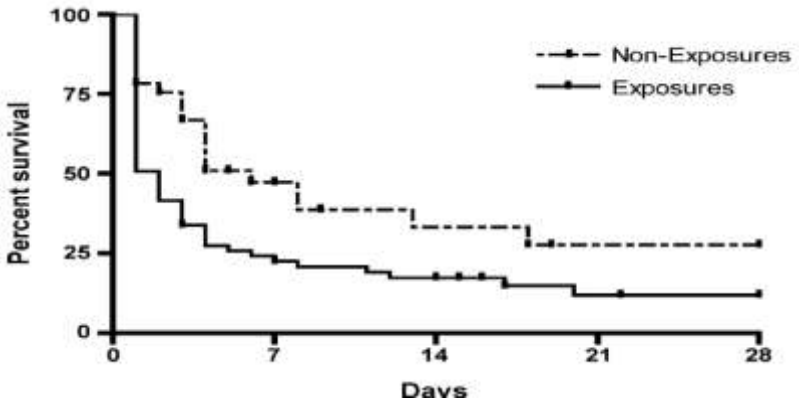


Figure 2. Myocardial blood flow and left ventricular ejection fraction at both baseline **(solid bar)** and at 5 h **(open bar)** after resuscitation. No difference in myocardial blood is seen, but a large decrease is seen in ejection fraction. *$p \leq 0.05$.

- 10-15m arrest & defibrillation
- Acute decrease in LVEF peaks at 24h, improves at 24-48h.

Kern. J Am Coll Cardiol 1996;28:232-40
Laurent. J Am Coll Cardiol 2002;40:2110-6

hypotension



- SBP < 100mmHg on two episodes within first 6 hours independently associated with death

Resuscitation 2008;79:410-6.

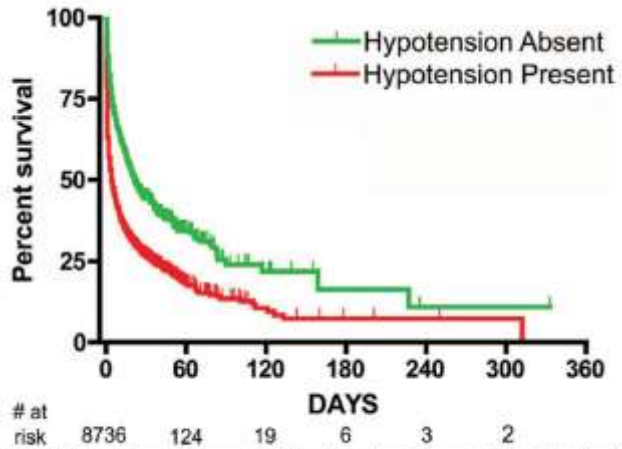


Figure 1. Kaplan-Meier survival curves for patients with Hypotension Present and Hypotension Absent after return of spontaneous circulation from cardiac arrest (with censoring). The survival fractions diverged significantly by log-rank test ($p < .001$).

•Hypotension in first hour independently associated with death

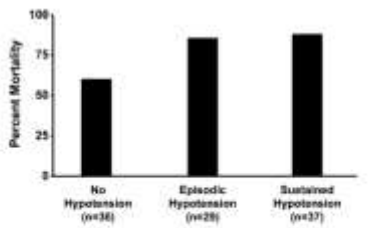


Figure 3 Percent in-hospital mortality for subjects with no hypotension, episodic hypotension, and sustained hypotension as defined by the criteria from Jones et al.[14,22]

Crit Care Med 2009;37:2895-903

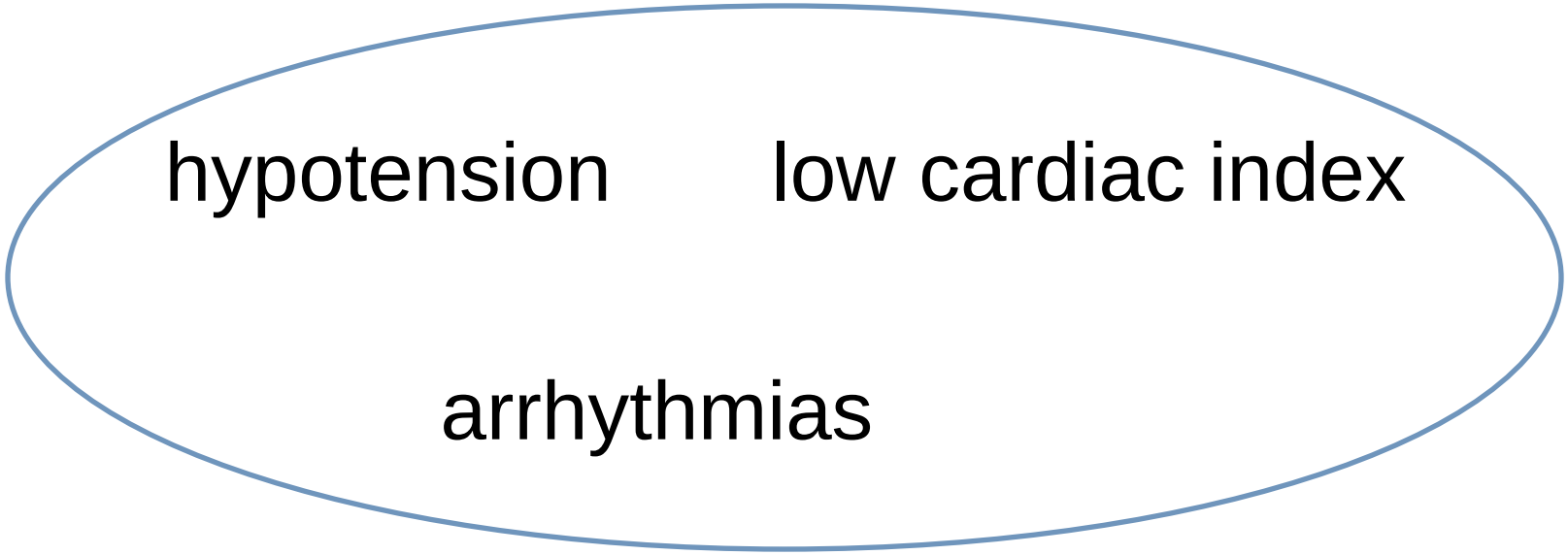
Post-arrest hypertension in humans

- Higher systolic pressure at 5, 10, 20, and 60 minutes was associated with good neurological outcome
- Relationship preserved after controlling for age, gender, arrest time, CPR time, and comorbid conditions

Crit Care Med 1999;27(S):A29

Haemodynamic management

- Post-resuscitation myocardial dysfunction causes haemodynamic instability,



Haemodynamic management

- early echocardiography in all patients
- Post-resuscitation myocardial dysfunction
- inotropic support
- vasoplegia
- severe vasodilation

Haemodynamic management

- Noradrenaline, with or without Dobutamine, and
- Fluid

most effective treatments

Haemodynamic management

- Treatment may be guided by
- blood pressure
- heart rate
- urine output
- rate of plasma lactate clearance
- central venous oxygen saturation

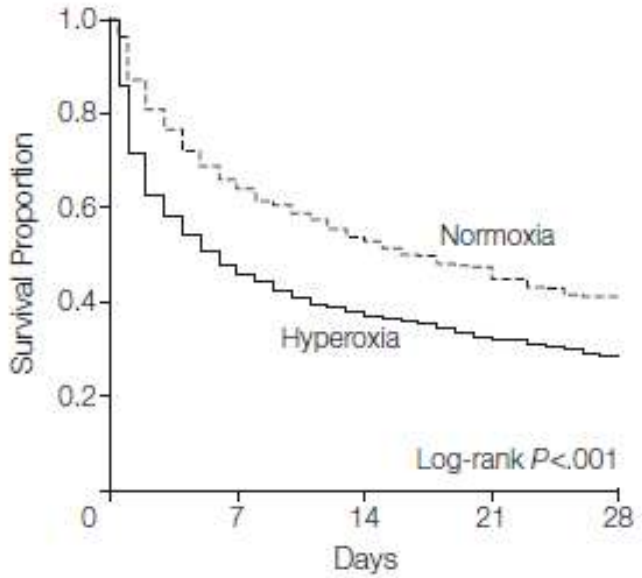
BP Goals after CA

- **Cerebral perfusion concerns balanced against risks to the heart**
- No randomized human data to support inducing hypertension
- Europe tends to favor empiric MAP 80-90
- Blood pressure can be titrated to specific hemodynamic endpoints, or to directly measured CNS targets

3 groups…

- *First* ABG
- Hypoxia:
  - PaO2<60mmHg
- Normoxia
  - PaO2 60-299mmHg
- Hyperoxia
  - PaO2≥300mmHg

Figure. In-Hospital Death Between Hyperoxia and Normoxia



No. at risk

Normoxia	1171	514	236	129	83
Hyperoxia	1156	406	211	115	70

JAMA 2010;303:2165

The post-cardiac arrest syndrome

- Acidemia associated with cardiac arrest improves spontaneously when adequate ventilation and perfusion are restored.

Control of ventilation

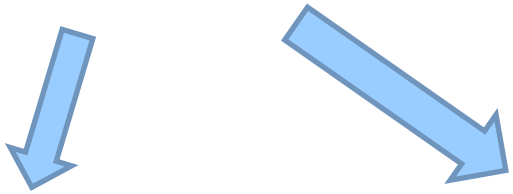
Consider

- tracheal intubation
- Sedation
- controlled ventilation

  in any patient with obtunded cerebral function

Control of ventilation

- Hypocarbia ⇨ cerebral vasoconstriction, it
- adjust ventilation to achieve normocarbia



- end-tidal CO_2 arterial blood gas

apply protective lung ventilation:

- tidal volume 6–8 mL kg^{-1} ideal body weight
- positive end expiratory pressure 4–8 cm H_2O

Airway and breathing

- Insert a gastric tube
- adequate doses of sedative
- neuromuscular blocking drug
- Continuous electroencephalography (EEG)
- chest radiograph

Airway and breathing
Control of oxygenation

- titrate the inspired O2 SPO2 94–98%
- Avoid hypoxaemia

Hyperoxia after Cardiac Arrest

Association Between Arterial Hyperoxia Following Resuscitation From Cardiac Arrest and In-Hospital Mortality

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Alan E. Jones, MD
Nathan I. Shapiro, MD, MPH
Mark G. Angelos, MD
Barry Milcarek, PhD
Krystal Hunter, MBA
Joseph E. Parrillo, MD
Stephen Trzeciak, MD, MPH
for the Emergency Medicine Shock Research Network (EMShockNet) Investigators

Context Laboratory investigations suggest that exposure to hyperoxia after resuscitation from cardiac arrest may worsen anoxic brain injury; however, clinical data are lacking.

Objective To test the hypothesis that postresuscitation hyperoxia is associated with increased mortality.

Design, Setting, and Patients Multicenter cohort study using the Project IMPACT critical care database of intensive care units (ICUs) at 120 US hospitals between 2001 and 2005. Patient inclusion criteria were age older than 17 years, nontraumatic cardiac arrest, cardiopulmonary resuscitation within 24 hours prior to ICU arrival, and arterial blood gas analysis performed within 24 hours following ICU arrival. Patients were divided into 3 groups defined a priori based on PaO_2 on the first arterial blood gas values obtained in the ICU. Hyperoxia was defined as PaO_2 of 300 mm Hg or greater; hypoxia, PaO_2 of less than 60 mm Hg (or ratio of PaO_2 to fraction of inspired oxygen <300); and normoxia, not classified as hyperoxia or hypoxia.

Main Outcome Measure In-hospital mortality.

Results Of 6326 patients, 1156 had hyperoxia (18%), 3999 had hypoxia (63%), and 1171 had normoxia (19%). The hyperoxia group had significantly higher in-hospital mortality (732/1156 [63%; 95% confidence interval {CI}, 60%-66%]) compared with the normoxia group (532/1171 [45%; 95% CI, 43%-48%]; proportion difference, 18% [95% CI, 14%-22%]) and the hypoxia group (2297/3999 [57%; 95% CI, 56%-59%]; proportion difference, 6% [95% CI, 3%-9%]). In a model controlling for potential confounders (eg, age, preadmission functional status, comorbid conditions, vital signs, and other physiological indices), hyperoxia exposure had an odds ratio for death of 1.8 (95% CI, 1.5-2.2).

Conclusion Among patients admitted to the ICU following resuscitation from cardiac arrest, arterial hyperoxia was independently associated with increased in-hospital mortality compared with either hypoxia or normoxia.

JAMA. 2010;303(21):2165-2171

SUDDEN CARDIAC ARREST IS THE most common lethal consequence of cardiovascular disease. Even if return of spontaneous circulation (ROSC) from cardiac arrest is achieved, approximately 60% of patients will not survive to hospital discharge.[1,2] The high mortality is attributed to the postcardiac arrest syndrome, which involves global ischemia-reperfusion injury, myocardial stunning, and anoxic brain injury. The recent success of therapeutic hypother-

JAMA 2010;303:2165

Hyperoxia in post-resuscitation CA care questioned!

- “Normoxic resuscitation”
- “Lowest FiO2 to generate an SpO2 of 95-99%

- Received consideration in new AHA and ACLS guidelines

- Turn down the FiO_2 if tolerated!

  (but be careful)

Circulation, Coronary reperfusion

- Acute coronary syndrome (ACS) is a frequent cause of out-of-hospital cardiac arrest (OHCA)
- Early percutaneous coronary intervention (PCI), is feasible in patients with ROSC after cardiac arrest.

PCI following ROSC with ST-elevation

- post-ROSC electrocardiogram (ECG) more than 80% will have an acute coronary lesion
- ST segment elevation (STE)
- Left bundle branch block (LBBB)
- Early invasive management is beneficial in STE patients.

PCI following ROSC with ST-elevation

- Immediate angiography and PCI when indicated should be performed in resuscitated OHCA patients whose initial ECG shows ST-elevation, even if they remain comatose
- Do not use level of consciousness after cardiac arrest caused by suspected acute STEMI to determine whether a person is eligible for coronary angiography

Percutaneous coronary intervention following ROSC without ST-elevation

- patient age
- duration of CPR
- haemodynamic instability
- presenting cardiac rhythm
- neurological status upon hospital arrival
- likelihood of cardiac aetiology

Indications and timing of computed tomography (CT) scanning

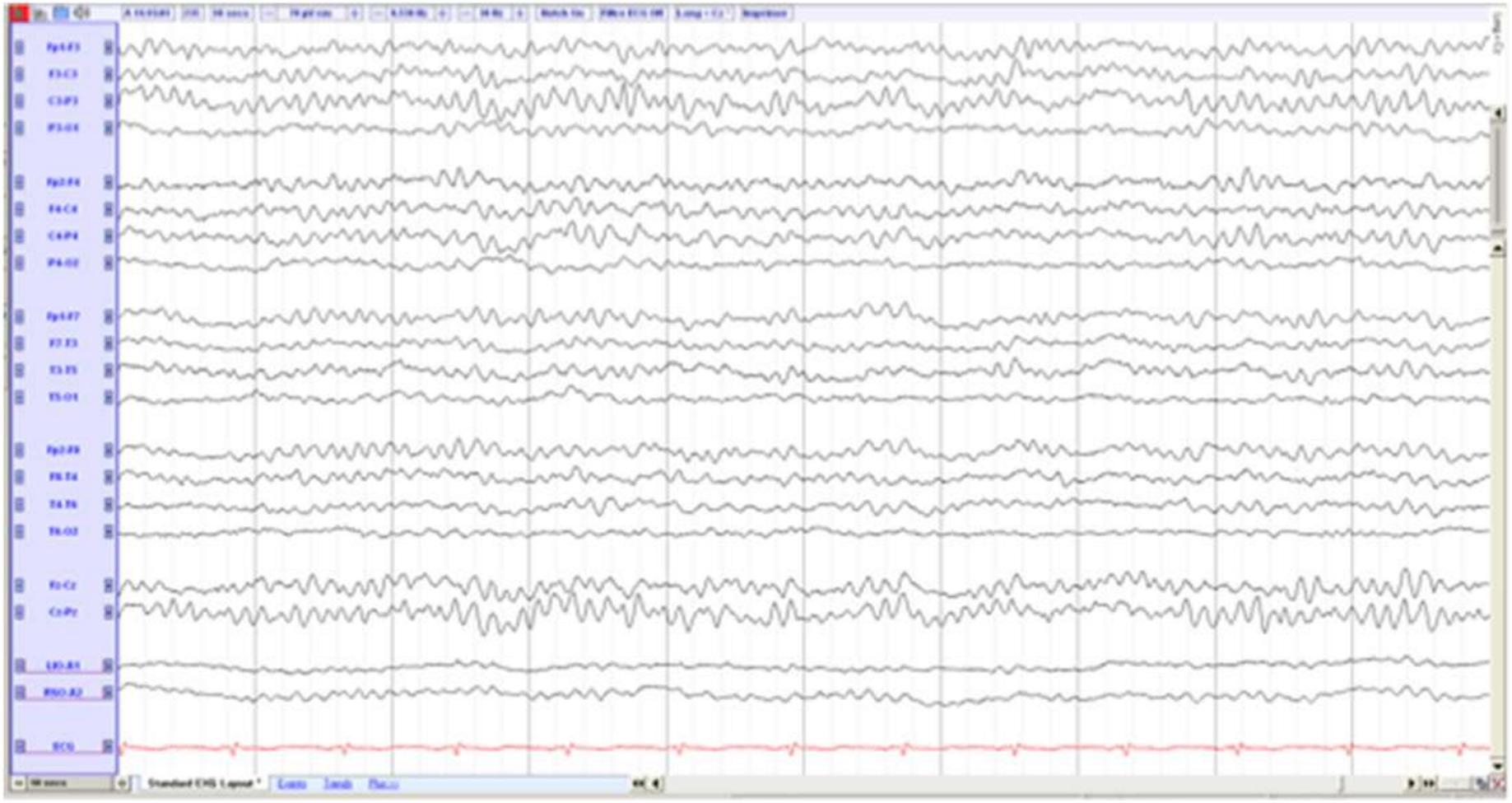
- In the absence of signs or symptoms suggesting a neurological or respiratory cause or if there is clinical or ECG evidence of myocardial ischaemia, undertake coronary angiography first, followed by CT scan in the absence of causative lesions

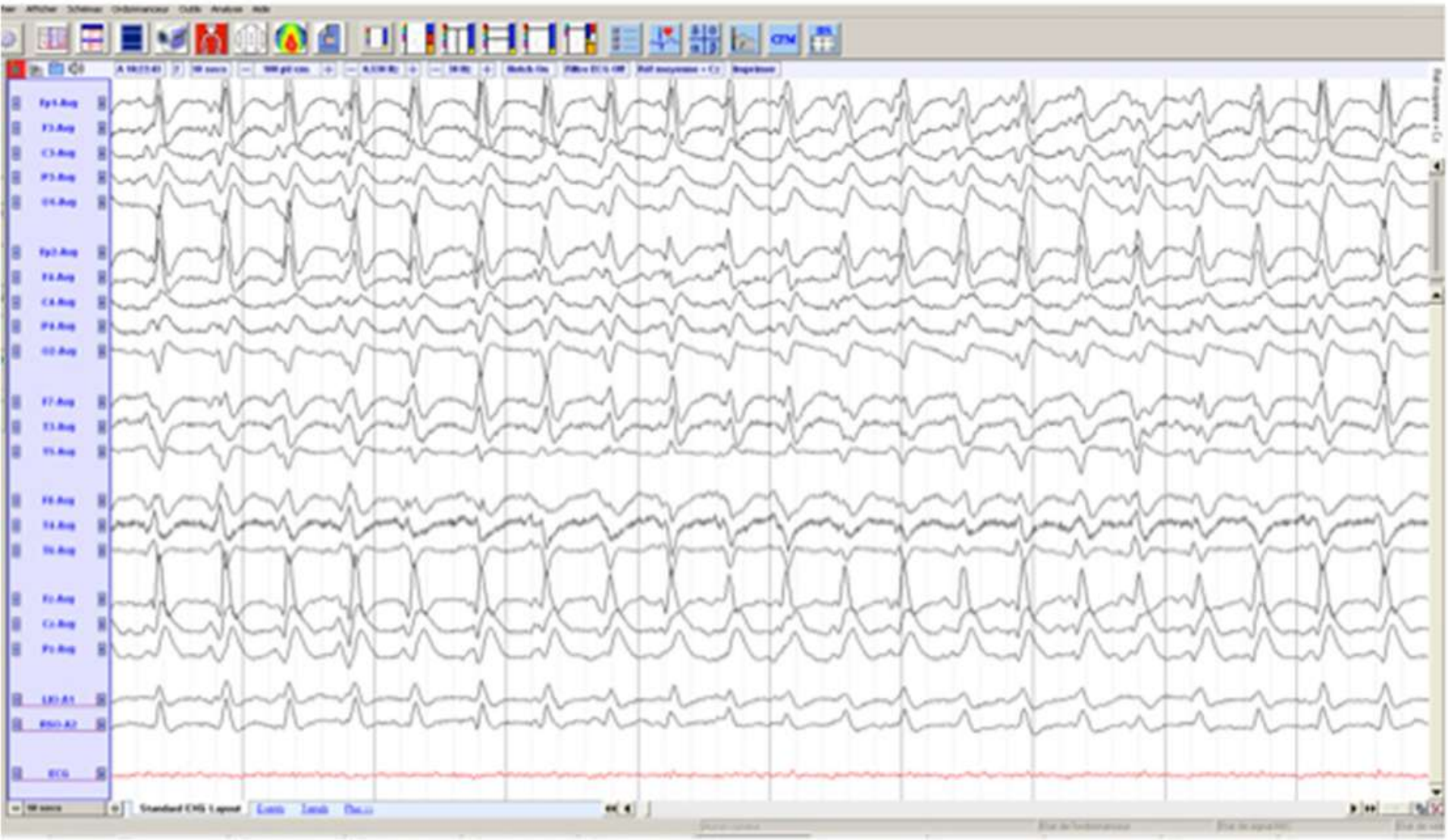
Control of seizures

- Seizures are common after cardiac arrest
- approximately one-third of patients who remain comatose after ROSC
- Myoclonus is most common and occurs in 18–25%
- focal or generalised tonic-clonic seizures or a combination of seizure types.

Control of seizures

- Routine seizure prophylaxis in post-cardiac arrest patients is not recommended because of the risk of adverse effects and the poor response to anti-epileptic drugs among patients with clinical and electrographic seizures.





Glucose control

- There is a strong association between high blood glucose after resuscitation from cardiac arrest and poor neurological outcome.
- Do not implement strict glucose control in adult patients with ROSC after cardiac arrest because it increases the risk of hypoglycaemia.

Immediate treatment

Airway and Breathing

- Maintain SpO_2 94 – 98%
- Advanced airway
- Waveform capnography
- Ventilate lungs to normocapnia

Circulation

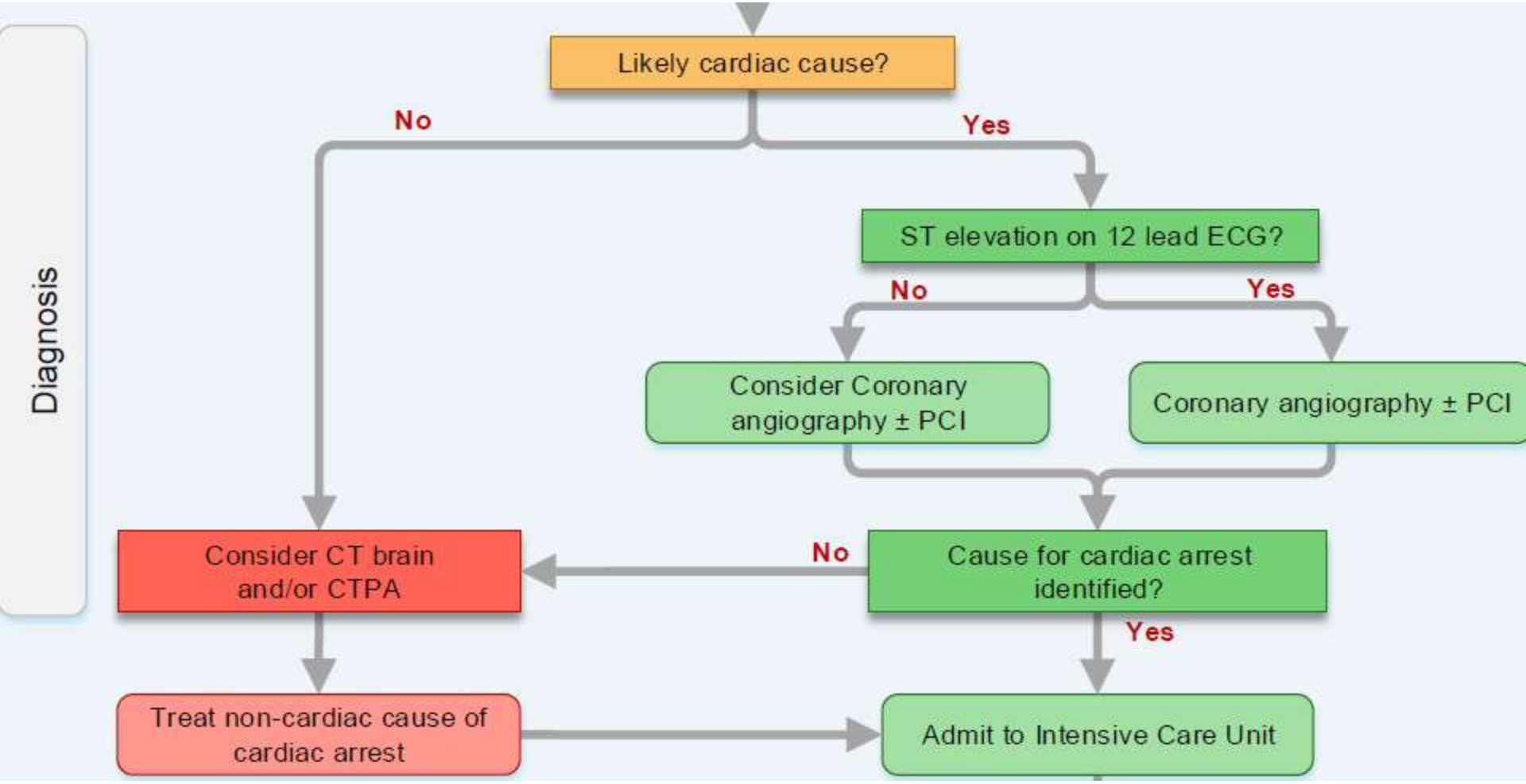
- 12-lead ECG
- Obtain reliable intravenous access
- Aim for SBP > 100 mmHg
- Fluid (crystalloid) – restore normovolaemia
- Intra-arterial blood pressure monitoring
- Consider vasopressor/ inotrope to maintain SBP

Control temperature

- Constant temperature 32°C – 36°C
- Sedation; control shivering

Resuscitation Council (UK)

GUIDELINES 2015

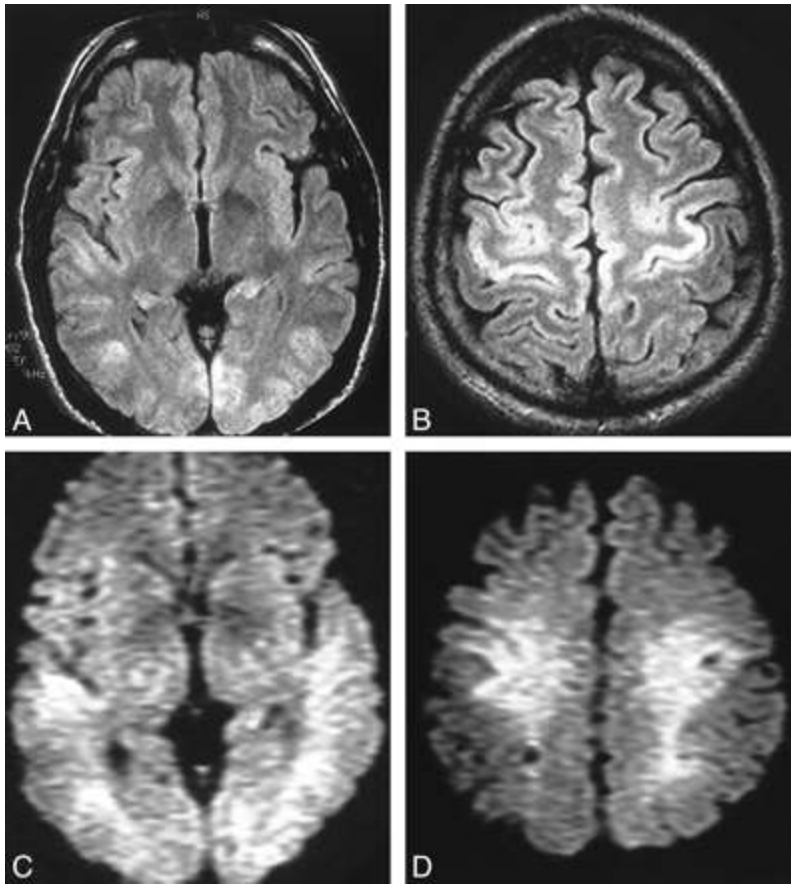


The post-cardiac arrest syndrome

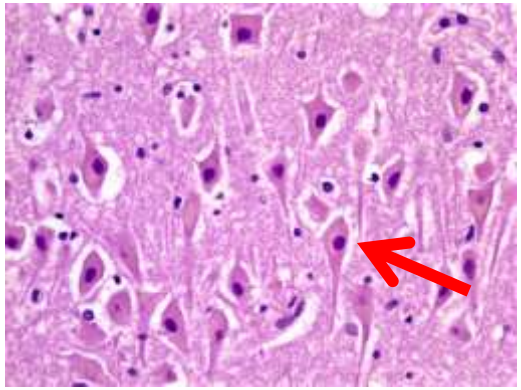
- restoration of blood pressure and improvement in gas exchange do not ensure survival and functional recovery

optimising neurological recovery

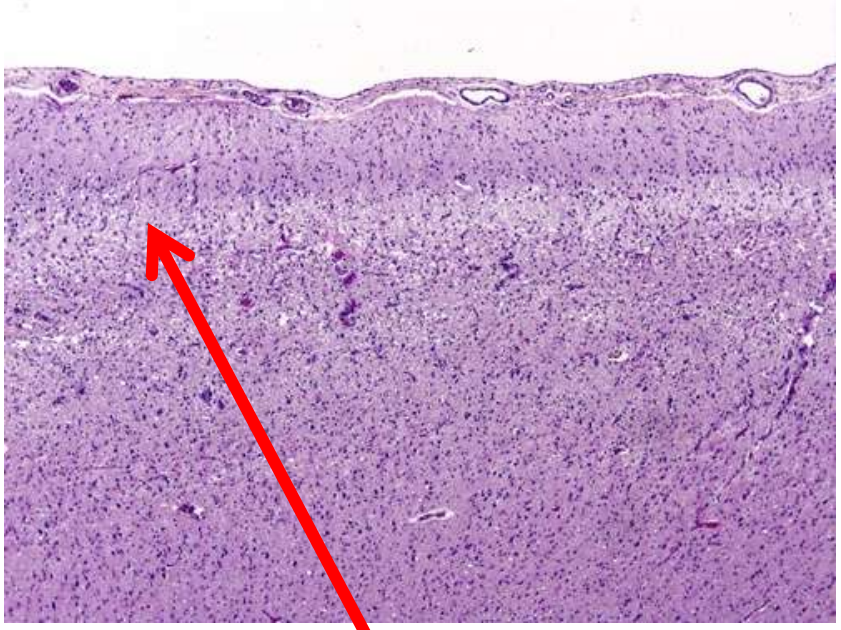
Cardiac arrest associated brain injury “CAABI”

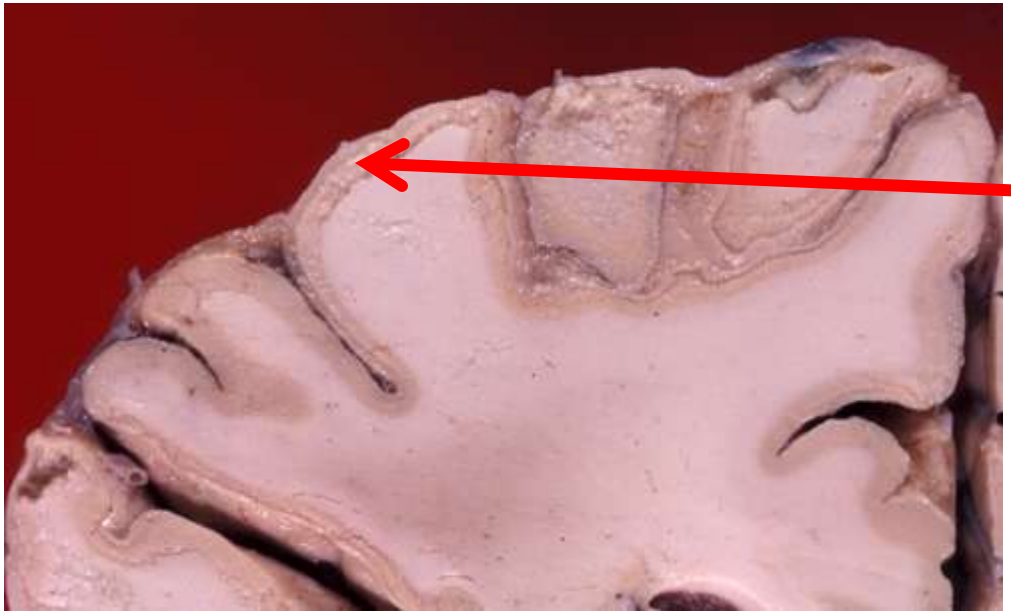


- “No flow” affects the most metabolically active areas of brain
  - Cortex
  - Basal ganglia
  - Cerebellum
- “Low flow” affects the watershed areas between vascular territories



Shrunken eosinophilic neuron (**anoxic neuron**) is the hallmark of HIE





Pseudolaminar necrosis

http://www.neuropathologyweb.org/chapter2/chapter2aHIE.html

secondary brain injury…

- Uncontrolled seizure activity
- Hypotension, hypoperfusion
  - Postresuscitation syndrome
  - ICP crisis
  - Autoregulatory failure
- Fever
- Re-arrest
- Hypoxia
- Derangements of glucose metabolism

Neurology 2008;72:744

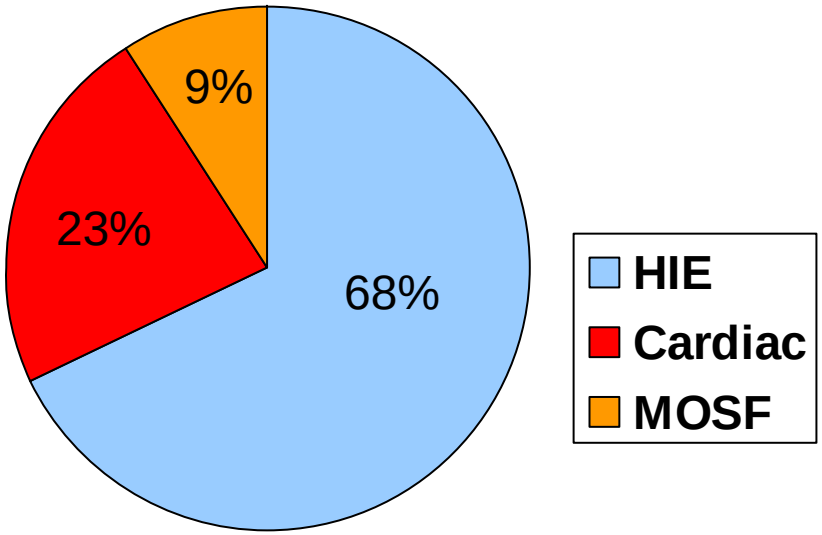
Mechanisms of brain injury in circulatory arrest

- Primary Injury:
  - "Energy failure" due to ATP depletion
- Secondary injury:
  - Loss of transcellular electrolyte gradients
    - Ca^{+}, Na^{+}, Cl^{-} enter, K^{+} exits cell
    - Water follows Na^{+} into cells causing cytotoxic edema
  - Lipid peroxidases damage membranes
  - Neurotransmitter release causes excitotoxicity
  - Activation of apoptotic pathways
  - Microvascular thrombosis
  - Reperfusion injury

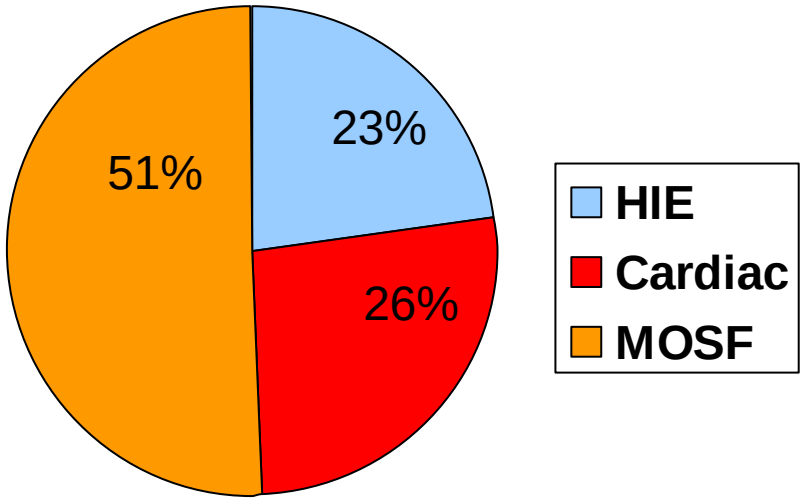
6-72h

From what do they die…?

Cause of Death in OHCA



Cause of death in IHCA



Laver. Intensive Care Med 2004;30:2126

Post-resuscitation care

- The brain injury is the leading cause of death, and must be addressed,

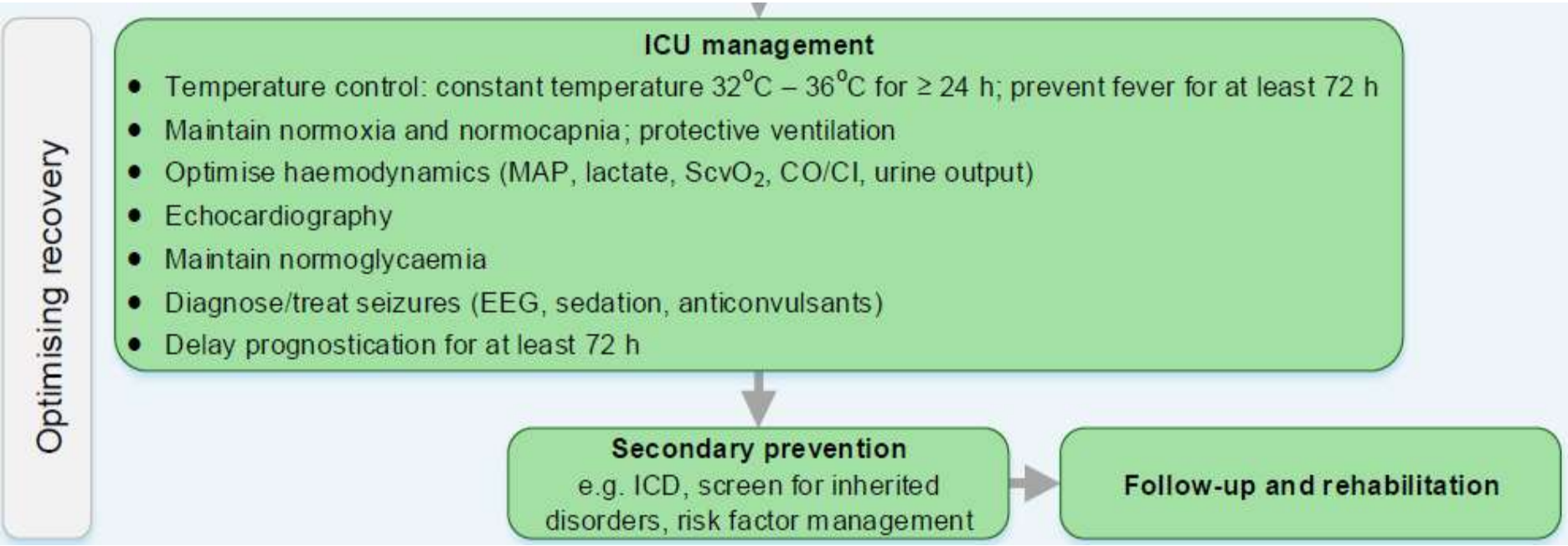
  but…

- Hemodynamic support is a critical element of the neurological resuscitation

Post-arrest care is as important as intra-arrest care

- Once we've achieved ROSC our job is not over
- Good post-arrest care involves maintaining blood pressure
- cerebral perfusion,
- adequate sedation,
- cooling and preventing hyperthermia,
- considering antiarrhythmic medications,
- optimization of tissue oxygen delivery while avoiding hyperoxia, getting patients to PCI who need it,
- looking for and treating the underlying cause.

Targeted Temperature Management


Optimising recovery
ICU management
Temperature control: constant temperature 32°C – 36°C for ≥ 24 h; prevent fever for at least 72 h
Maintain normoxia and normocapnia; protective ventilation
Optimise haemodynamics (MAP, lactate, ScvO2, CO/CI, urine output)
Echocardiography
Maintain normoglycaemia
Diagnose/treat seizures (EEG, sedation, anticonvulsants)
Delay prognostication for at least 72 h
Secondary prevention
e.g. ICD, screen for inherited disorders, risk factor management
Follow-up and rehabilitation

Cerebral perfusion

- immediately after ROSC there is a short period of multifocal cerebral no-reflow followed by transient global cerebral hyperaemia lasting 15–30 min.
- This is followed by up to 24 h of cerebral hypoperfusion while the cerebral metabolic rate of oxygen gradually recovers

After asphyxial cardiac arrest

- brain oedema may occur transiently after ROSC but it is rarely associated with clinically relevant increases in intracranial pressure.
- after ROSC, maintain mean arterial pressure near the patient's normal level.

THE USE OF HYPOTHERMIA AFTER CARDIAC ARREST

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Baltimore, Maryland*

Anesthesia and Analgesia 1959;38 (6): 423

History

- 1803 "Russian Method of Resuscitation" consisted of burying the victim of a cardiac arrest in snow hoping for ROSC

DATA FROM TWENTY-SEVEN CASES OF CARDIAC ARREST

Table

Case No.	Age	Sex	Site of arrest and date	Operation or episode at arrest	Neurological status after arrest	Interval from arrest to hypothermia	Average temperature during hypothermia, Centigrade	Duration of hypothermia, hr.	Outcome
14	64	F	Recovery room 6/24/57	Postcholecystectomy, 4 hr.	None				Lived; no residual
15	84	F	Operating room 11/21/57	General anesthesia; incarcerated hernia	None				Lived; no residual
16	1	F	Bronchoscopy 11/28/57	Bronchoscopy; local anesthesia	Severe	1 hr.	30°	3	Died 4 hr.
17	45	F	Operating room 6/10/58	General anesthesia; breast biopsy	Severe	1 hr.	32°	24	Died 24 hr.
18	53	M	Operating room 2/7/58	General anesthesia; thoracotomy	Severe	1 hr.	31°	48	Died 3 days
19	55	M	Operating room 6/16/58	General anesthesia; hernia repair	Severe	3 hr.	30°	8 days	Died 9 days; did not respond
20	57	M	Operating room 9/24/58	General anesthesia; suprapubic prostatectomy	Severe	1 hr.	30°	77	Died 3 days
21	58	M	Operating room 8/18/58	General anesthesia; pneumonectomy	Severe	6 hr.	31°	84	Died 5 days
22	3	M	X-ray department 1/22/57	General anesthesia; bronchogram	Severe	2 hr. 40 min.	31°	36	Lived; no residual
23	6	F	Bronchoscopy 8/12/58	General anesthesia; bronchoscopy	Severe	1 hr.	32°	48	Lived; no residual
24	9	F	Accident room 8/20/57	Asthmatic attack	Severe	1 hr. 30 min.	30°	34	Lived; no residual
25	10	M	Operating room 4/5/58	General anesthesia; rectal pull-through	Severe	1 hr. 30 min.	32°	72	Lived; no residual
26	38	M	Accident room 9/28/57	Pericardial tamponade	Severe	1 hr. 50 min.	32°	36	Lived; no residual
27	39	F	Accident room 11/16/57	Stab wound of chest	Severe	3 hr.	31°	48	Lived; no residual

Anesthesia and Analgesia 1959;38 (6): 423

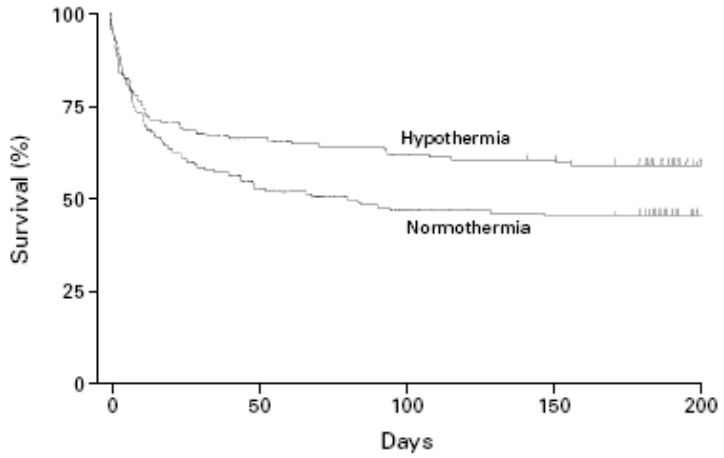
Clinical evidence for TH after CA

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*



- Largest RCT of TH in OHCA survivors
  - 275 patients randomized to TH or routine care
  - Europe 1996-2001
- **Absolute 16% increase in chance of a good neurological outcome**
- Absolute 14% decrease in 6 month mortality

N Engl J Med 2002;346:549-56

Clinical evidence for TH after CA

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.

N Engl J Med 2002;346:549-56

Clinical evidence for TH after CA

TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

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

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

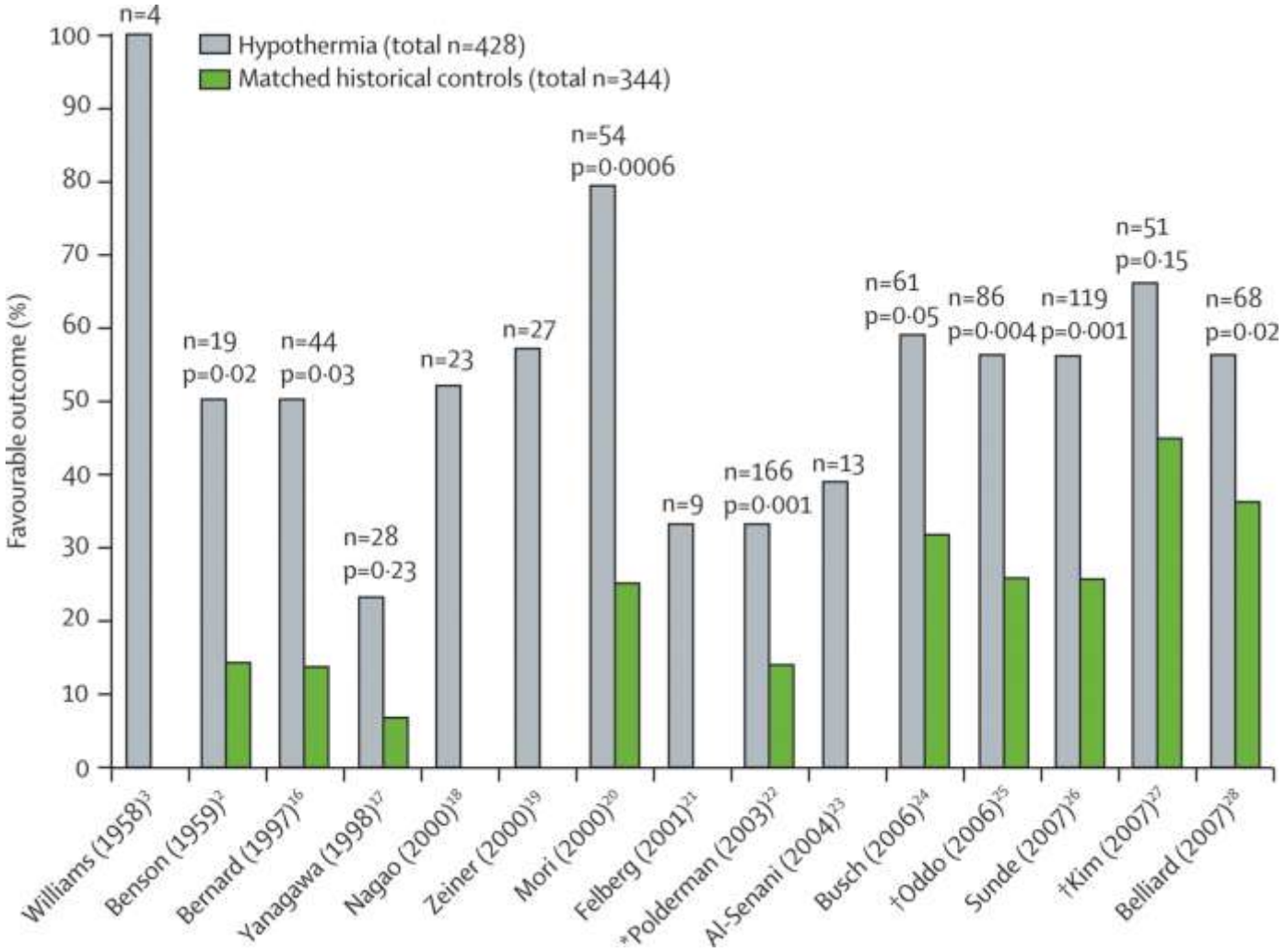
New Engl J Med 2002; 346:557-63

- Australian RCT

1996-1999

- **TH: GNO 49%, routine care good outcome: 26%**

Nonrandomized data



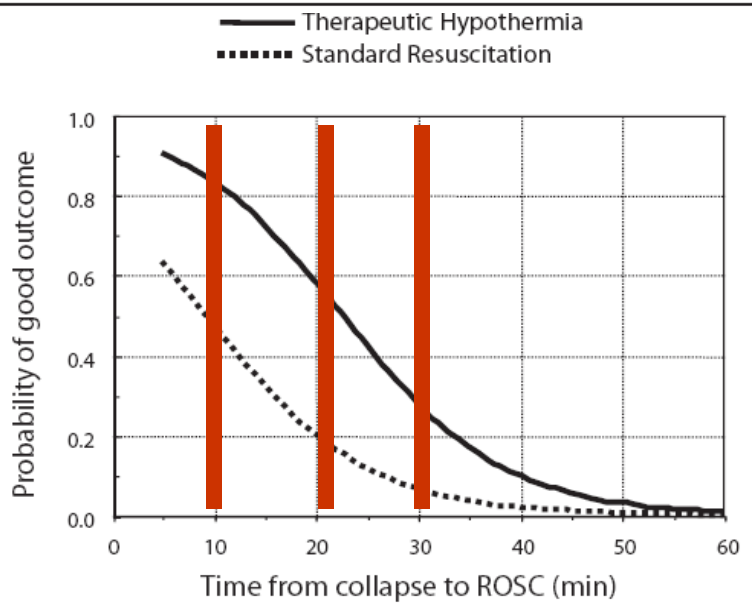
Polderman. Lancet 2008, 371:1955-1969.

Lausanne

- 55 VT/VF OHCA treated with TH 2002-2004
- Compared to historical controls 1999-02
- Similar DT, severity of illness
- CPC 1-2: 56% vs. 26% pre-TH

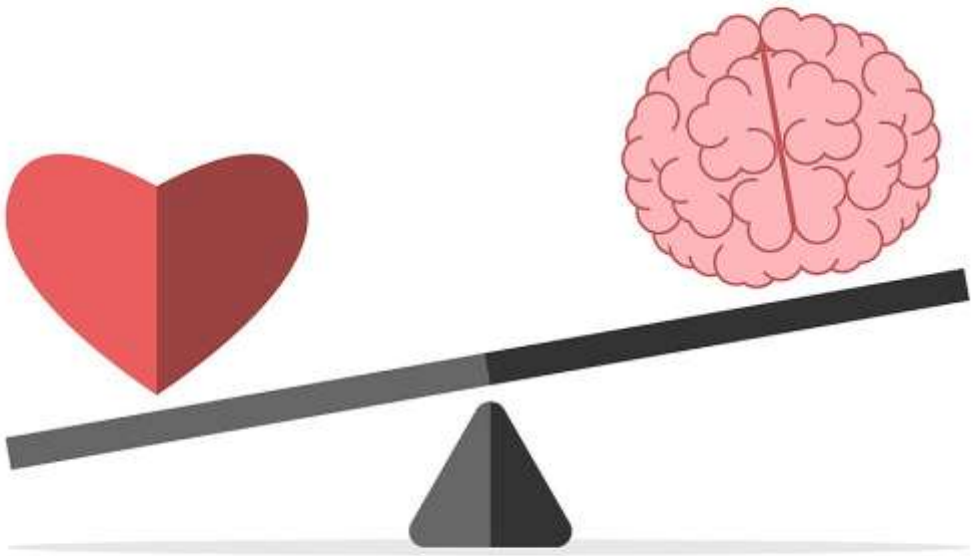
Table 4. Outcome, at hospital discharge, of comatose patients with out-of-hospital cardiac arrest (initial rhythm: ventricular fibrillation)

	Outcome				
Treatment Group	CPC 1 Total Recovery	CPC 2 Moderate Disability	CPC 3 Severe Disability	CPC 4 Vegetative State	CPC 5 Death
Therapeutic hypothermia	18/43 (41.9)	6/43 (13.9)	2/43 (4.7)	0/43 (0)	17/43 (39.5)
Standard resuscitation	6/43 (14.0)	5/43 (11.6)	8/43 (18.6)	0/43 (0)	24/43 (55.8)



Effect of the implementation of a therapeutic hypothermia protocol on neurological outcome after out-of-hospital VF/VT arrest

-Crit Care Med 2006;34:1865



Risks

- Infections
- Bleeding
- Need for sedation

Benefits

- Strongly neuroprotective
- Decreased mortality
- Better neurological outcome

N Engl J Med 2002;346:549-56

What are the risks?

TABLE 4. COMPLICATIONS DURING THE FIRST SEVEN DAYS AFTER CARDIAC ARREST.*

COMPLICATION	NORMOTHERMIA	HYPOTHERMIA
	no./total no. (%)	
Bleeding of any severity†	26/138 (19)	35/135 (26)
Need for platelet transfusion	0/138	2/135 (1)
Pneumonia	40/137 (29)	50/135 (37)
Sepsis	9/138 (7)	17/135 (13)
Pancreatitis	2/138 (1)	1/135 (1)
Renal failure	14/138 (10)	13/135 (10)
Hemodialysis	6/138 (4)	6/135 (4)
Pulmonary edema	5/133 (4)	9/136 (7)
Seizures	11/133 (8)	10/136 (7)
Lethal or long-lasting arrhythmia	44/138 (32)	49/135 (36)
Pressure sores	0/133	0/136

*None of the comparisons between the two groups, performed with the use of Pearson's chi-square test, indicated significant differences.

†The sites of bleeding were mucous membranes, the nose, the urinary tract, the gastrointestinal tract, subcutaneous tissue, and skin, as well as intracerebral and intraabdominal sites.

- More infections
  - Lung
- more bleeding*
- Electrolyte shifts
- Clinically insignificant bradycardia
- Changes in drug metabolism

HCASG. NEJM 2002;346:549-56

TH after Cardiac Arrest

- **Clinical criteria for therapeutic hypothermia**
  - No more than **8 hours** have elapsed since the return of spontaneous circulation.
  - **Encephalopathy** is present, typically defined as the patient being unable to follow verbal commands.
  - There is **no life-threatening infection or bleeding**.
  - **Aggressive care is warranted** and desired by the patient or the patient's surrogate decision-maker
    - Terminal underlying disease
    - Impending cardiopulmonary collapse

What do I treat with therapeutic hypothermia?

- Cardiac Arrest
- Hepatic encephalopathy with cerebral edema
- Near hanging
- Neonatal asphyxia
- Elevated ICP, all causes
- Severe (Hunt and Hess IV-V) SAH with cerebral edema

Starting cooling early is better

Therapeutic Hypothermia After Out-of-Hospital Cardiac Arrest

Evaluation of a Regional System to Increase Access to Cooling

Michael R. Mooney, MD; Barbara T. Unger, RN; Lori L. Boland, MPH; M. Nicholas Burke, MD; Kalie Y. Kebed, BS; Kevin J. Graham, MD; Timothy D. Henry, MD; William T. Katsiyiannis, MD; Paul A. Satterlee, MD; Sue Sendelbach, PhD, RN, CCNS; James S. Hodges, PhD; William M. Parham, MD

Background—Therapeutic hypothermia (TH) improves survival and confers neuroprotection in out-of-hospital cardiac arrest (OHCA), but TH is underutilized, and regional systems of care for OHCA that include TH are needed.

Methods and Results—The Cool It protocol has established TH as the standard of care for OHCA across a regional network of hospitals transferring patients to a central TH-capable hospital. Between February 2006 and August 2009, 140 OHCA patients who remained unresponsive after return of spontaneous circulation were cooled and rewarmed with the use of an automated, noninvasive cooling device. Three quarters of the patients (n=107) were transferred to the TH-capable hospital from referring network hospitals. Positive neurological outcome was defined as Cerebral Performance Category 1 or 2 at discharge. Patients with non–ventricular fibrillation arrest or cardiogenic shock were included, and patients with concurrent ST-segment elevation myocardial infarction (n=68) received cardiac intervention and cooling simultaneously. Overall survival to hospital discharge was 56%, and 92% of survivors were discharged with a positive neurological outcome. Survival was similar in transferred and nontransferred patients. Non–ventricular fibrillation arrest and presence of cardiogenic shock were associated strongly with mortality, but survivors with these event characteristics had high rates of positive neurological recovery (100% and 89%, respectively). A 20% increase in the risk of death (95% confidence interval, 4% to 39%) was observed for every hour of delay to initiation of cooling.

Conclusions—A comprehensive TH protocol can be integrated into a regional ST-segment elevation myocardial infarction network and achieves broad dispersion of this essential therapy for OHCA. (*Circulation*. 2011;124:206-214.)

- Start cooling ASAP!
- For every hour delay to onset of cooling, mortality increased by 20%!!

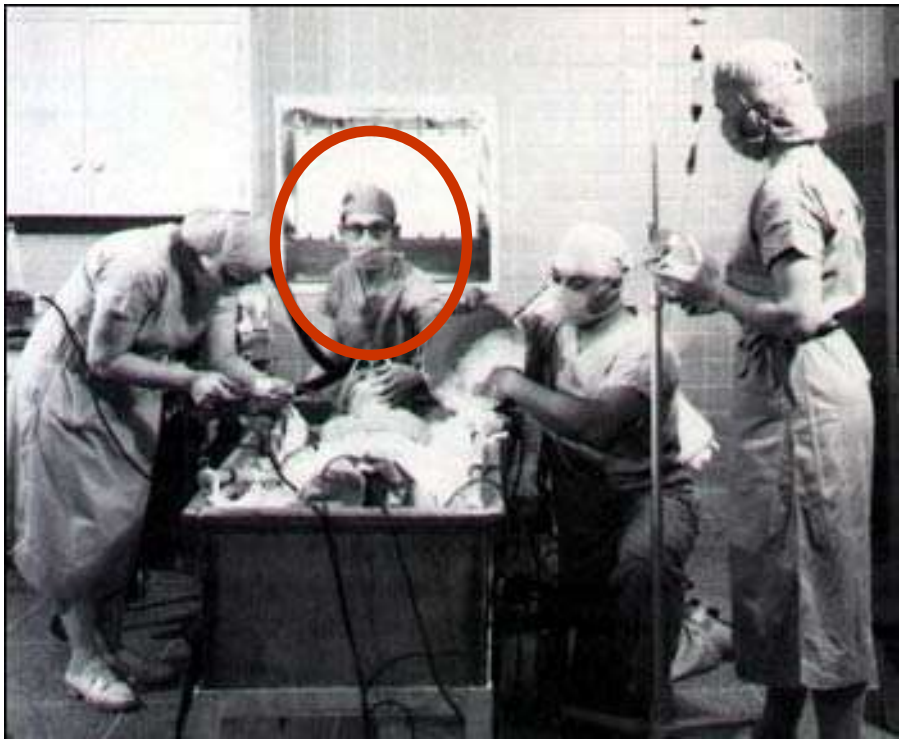
Basics of Therapeutic Hypothermia

- There are 3 phases of treatment:
  - **Induction**
  - **Maintenance**
  - **Decooling**

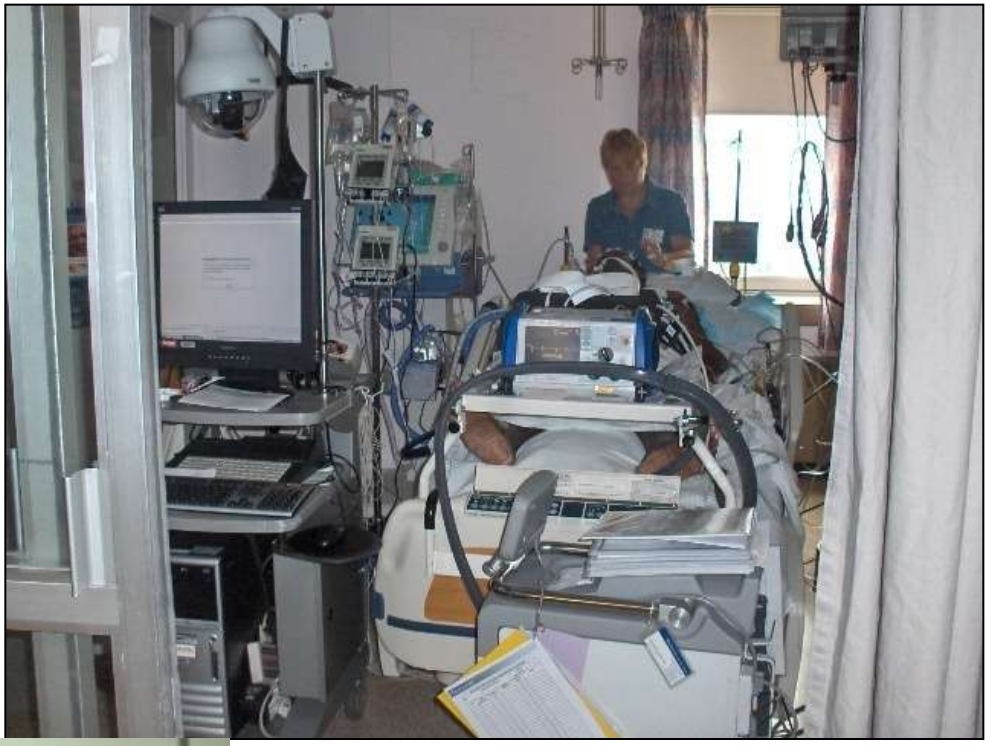
Induction

- Rapidly bring the temperature to 32-36C
- Sedate with propofol or midazolam during TH
- Paralyze to suppress heat production

How to cool…



Baltimore, 1955



Portland, Maine, 2006

Cold IVF

- **Polderman 2005**
  - 110 patients, 2-3L over 50’
  - 36.9°C to 34.6°C, **MAP increased by 15mmHg, no pulmonary edema**

Bernard 2003

- 22 patients 30cc/kg LR at 4°C over 30 min: 35.5°C to 33.8°C **Improvements in MAP, renal function, no pulmonary edema**

	Before Cooling	During Cooling	*p* Value
Medications, mg/hr			
Dopamine, n = 54	17.4 ± 12.0	10.2 ± 9.2	<.01
Norepinephrine, n = 56	0.42 ± 0.24	0.22 ± 0.18	.01
Dobutamine, n = 24	34.1 ± 32.2	32.2 ± 41.3	NS
Enoximone, n = 22	3.2 ± 3.6	3.0 ± 3.0	.13

Polderman. Crit Care Med 2005;33:2744
Bernard. Resuscitation 2003;56:9

Cold IVF

TABLE 3. Echocardiographic Measurements

	Baseline	1 Hour After Infusion	*P*
EF, %	34.1±18.6	39.6±20.6	0.09
E/E′	9.1±6	7.4±3.4	0.11
Pulmonary artery pressure, mm Hg	36.2±15	34.0±14	0.74
Central venous pressure, mm Hg	8.9±5.9	8.4±5.4	0.7

- 2-3L of Ringers or Saline at 4C decreases body temperature
  - No effect on LVEF by echo
  - Improved hemodynamic indices

Kim. Circulation 2005;112:715

Induction: how to cool

- **Monitor core temperature**
  - Bladder, esophagus, or central venous/pulmonary arterial
- **Cold fluid**
  - 30cc/kg LR or 0.9%NS over 30 minutes
    - 2-2.5C temperature reduction
  - No adverse cardiovascular results
  - Rare to cause pulmonary edema
- **Ice packs and cooling mats**
  - Effective, but difficult to control rate of temperature change
  - Overcooling is dangerous

Induction: how to cool

- **Commercial cooling devices**
  - Servo mechanism varies temperature of circulating water or air (prevents overcooling)
  - External (surface cooling) systems
    - Hydrogel heat exchange pads
    - Cold water circulating through plastic “suit”
    - Cold water immersion – awaiting safety data
  - Invasive (catheter based) systems
    - Heat exchange catheter in SVC or IVC
    - Plastic or metalic heat-exchange catheter

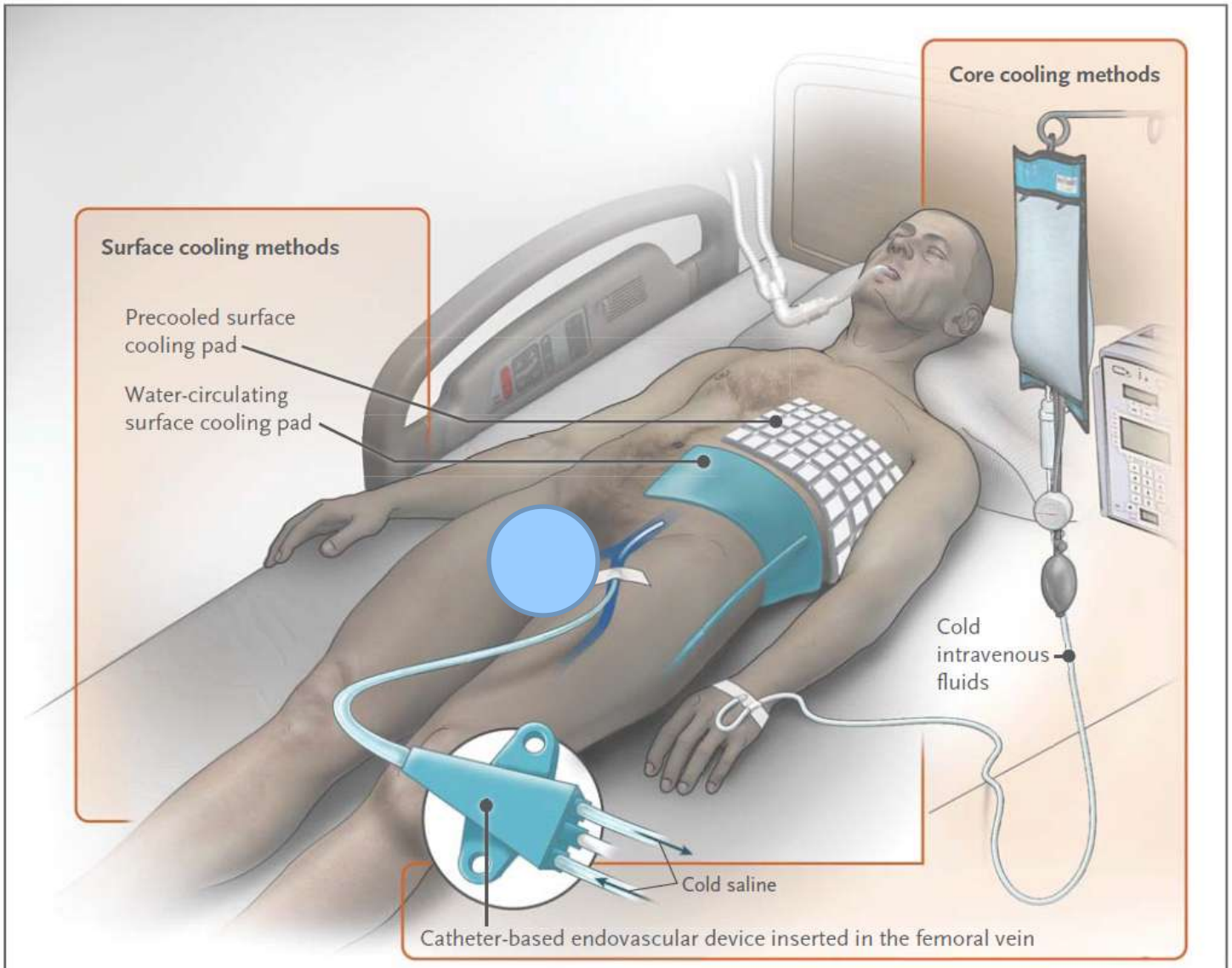


Figure 1. Cooling Methods Used in Clinical Practice.

Surface cooling methods include the use of precooled (refrigerated) surface cooling pads and water-circulating surface cooling pads. Core cooling methods include the infusion of cold intravenous fluids and the use of catheter-based endovascular devices.

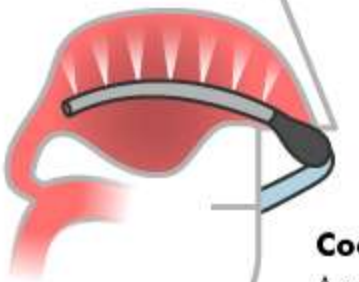
Holzer. New Engl J Med 2010;363:1256-64

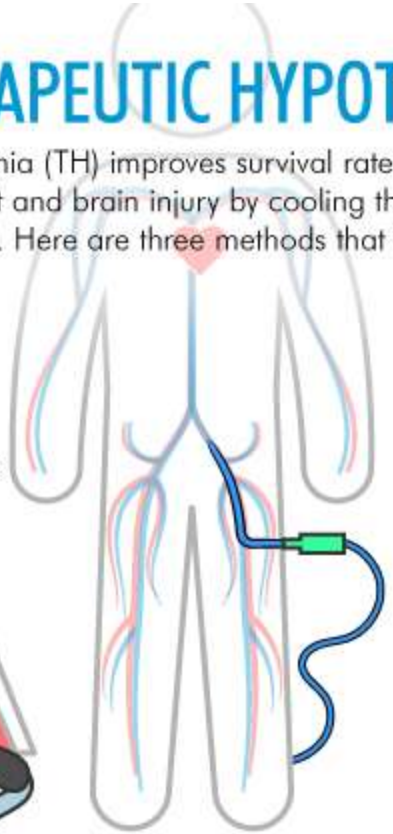
HOW THERAPEUTIC HYPOTHERMIA WORKS

Therapeutic hypothermia (TH) improves survival rates and brain function typically in cases of cardiac arrest and brain injury by cooling the body to be between 89.6 and 93.2 F (32 and 34 C). Here are three methods that hospitals use to induce TH.

Transnasal Evaporative Cooling

A tube inserted into the nasal cavity sprays a coolant mist, cooling the brain and bloodstream.



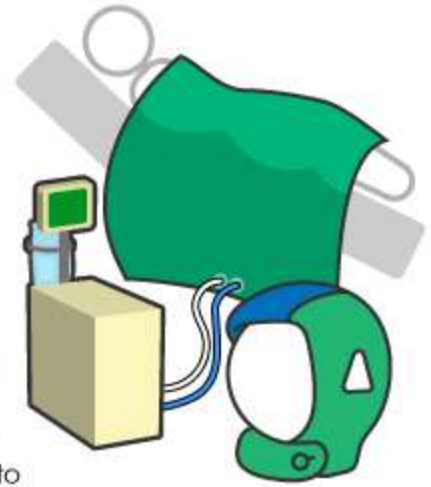


Cooling Catheter

A cooled saline solution is injected into the bloodstream through a catheter inserted into the femoral vein.

Water Blankets and Cooling Caps

Cooled water is circulated through specialized blankets and/or caps.

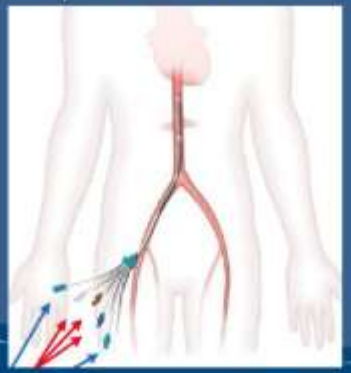


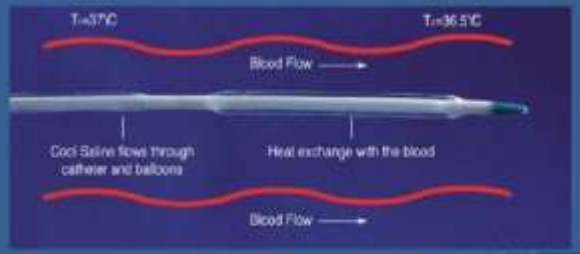
howstuffworks

Figure 1. Arctic Sun® 5000 Temperature Management System

Intravascular Cooling Systems

- Percutaneously placed central venous catheters
- Circulating cool or warm saline in a closed loop through the catheter's balloon
- Less shivering compared to surface devices
- Complication: Thrombosis





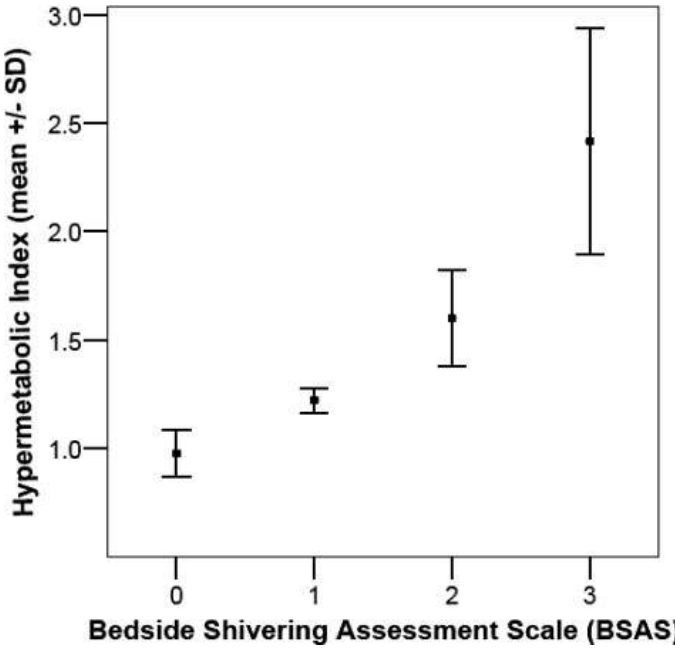
art | science | healing

Critical Care (2015) 19:103

UKHealthCare. Gill Heart Institute

Shivering

- Drives up systemic metabolic rate
  - Increased CO2 production
  - Increased O2 consumption
  - Major cardiac stressor
- Drives up cerebral oxygen consumption
  - Favors ischemia
- Uncomfortable



Score	Definition
0	**None:** no shivering noted on palpation of the masseter, neck, or chest wall
1	**Mild:** shivering localized to the neck and/or 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

Stroke. 2008 Dec;39(12):3242-7.

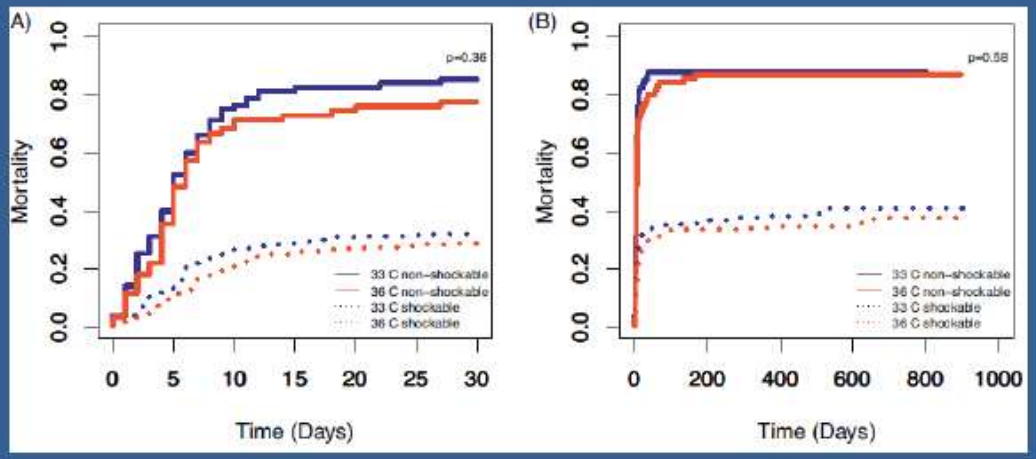
Management of shivering

- Neuromuscular blockade
  - Must give sedation, first!!
  - Vecuronium bolus 0.1mg/kg prn for shivering
- fentanyl
- Propofol
- Alpha blockade
  - Dexmedetomidine , clonidine
- acetaminophen
- Focal counterwarming
- Magnesium infusion (serum level 3-4mg/dl)

Maintenance

- maintain the goal temperature at 33-36
- Standard 12-24 hours
- Suppress shivering

Target temperature management of 33 °C and 36 °C in patients with out-of-hospital cardiac arrest with initial non-shockable rhythm – A TTM sub-study☆



	TTM33	TTM36	Hazard ratio or risk ratio (95% CI)	*p* value
Primary outcome: mortality at the end of trial, *n*/total (%)	81/96 (84)	69/82 (84)	0.75 (0.53–1.08)	0.12
Secondary outcome: neurologic outcome				
CPC 3–4, *n*/total (%)	84/96 (87)	70/82 (85)	0.67 (0.08–4.73)	0.69
Modified Rankin Scale 4–5, *n*/total (%)	84/96 (87)	70/82 (85)	0.67 (0.08–4.73)	0.69

- Comatose patients after OHCA with initial NSR continue to have a poor prognosis
- No effect of TTM at 33 ◦C compared to 36 ◦C in these patients

Mortality in Landmark Trials

	HACA (2002)	Bernard (2002)	TTM (2013)
Normothermia (37-38°C)	55%	68%	
32-34°C	41%	51%	50%
36°C			48%

- Fever is independently associated with an increased risk of adverse outcome

Hypothermia Protocol

- External cooling device (TheraKool)
- Sedation with Midazolam and Fentanyl
- Pancuronium to prevent shivering
- Target temperature of 32°C to 34°C for 24h
- Passive rewarming over 8h

De-cooling (rewarming)

- Most dangerous period:
- hypotension, cerebral edema, seizures
- Goal is to reach normal body temperature over 12-24h
- Stop sedation when normal body temperature is achieved

De-cooling

- Vasodilation causes hypotension
  - May require several liters IVF
- More shivering during this phase
- Inflammation increases at higher temperature
  - “post-resuscitation” syndrome
- Increased ICP
- Watch for hyperkalemia
  - Primarily problematic in renal failure
- SEIZURES

Rewarming

- At 28 hours after cardiac arrest,
- passive rewarming will commence
- cessation of active cooling and covering the patient with a blanket (warming blankets are NOT to be used for patients at 35°C-36°C).
- Rewarming should take place at a rate of approximately 0.25°C/hour,
- no greater than 0.5°C/hour to a target of 37.0°C over the next 8 hours (i.e. until 36 hours post cardiac arrest)

a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA
Faculty of Medicine

Vancouver CoastalHealth
Promoting wellness. Ensuring care

Rewarming and fever

- Prevalence up to 42% post CA[1]
- Rebound pyrexia seen in pts treated with TTM and those who were not[1]
- Post CA pyrexia associated with worse neurological outcomes[2]

1.Gebhardt et al Resuscitation 2013; 84: 1062-67

2.Leary et al Resuscitation 2013; 84: 1056-61

The influence of rewarming after therapeutic hypothermia on outcome after cardiac arrest

- patients who needed active rewarming after therapeutic hypothermia after CA did not have a higher risk for a poor outcome. In addition, neither speed of rewarming, nor development of fever had an effect on outcome

Resuscitation. 2012 Aug;83(8):996-1000
Bouwes A[1], Robillard LB

Physiological Aspects of Cooling

Initiation
- The optimal timing of induction remains uncertain although current evidence predominantly favors early cooling
- Cold infusion should be considered as first line for the induction phase

Maintenance
- Should use external cooling or an endovascular cooling device
- Requires an effective temperature monitoring control: eg. bladder, rectal, central venous or esophageal monitors
- Essential requirements:
  (1) Monitor fluid balance, electrolyte concentration, and drug dosage
  (2) Maintain blood glucose between 120-160mg/dL
  (3) Prevent infection
  (4) Treat shivering

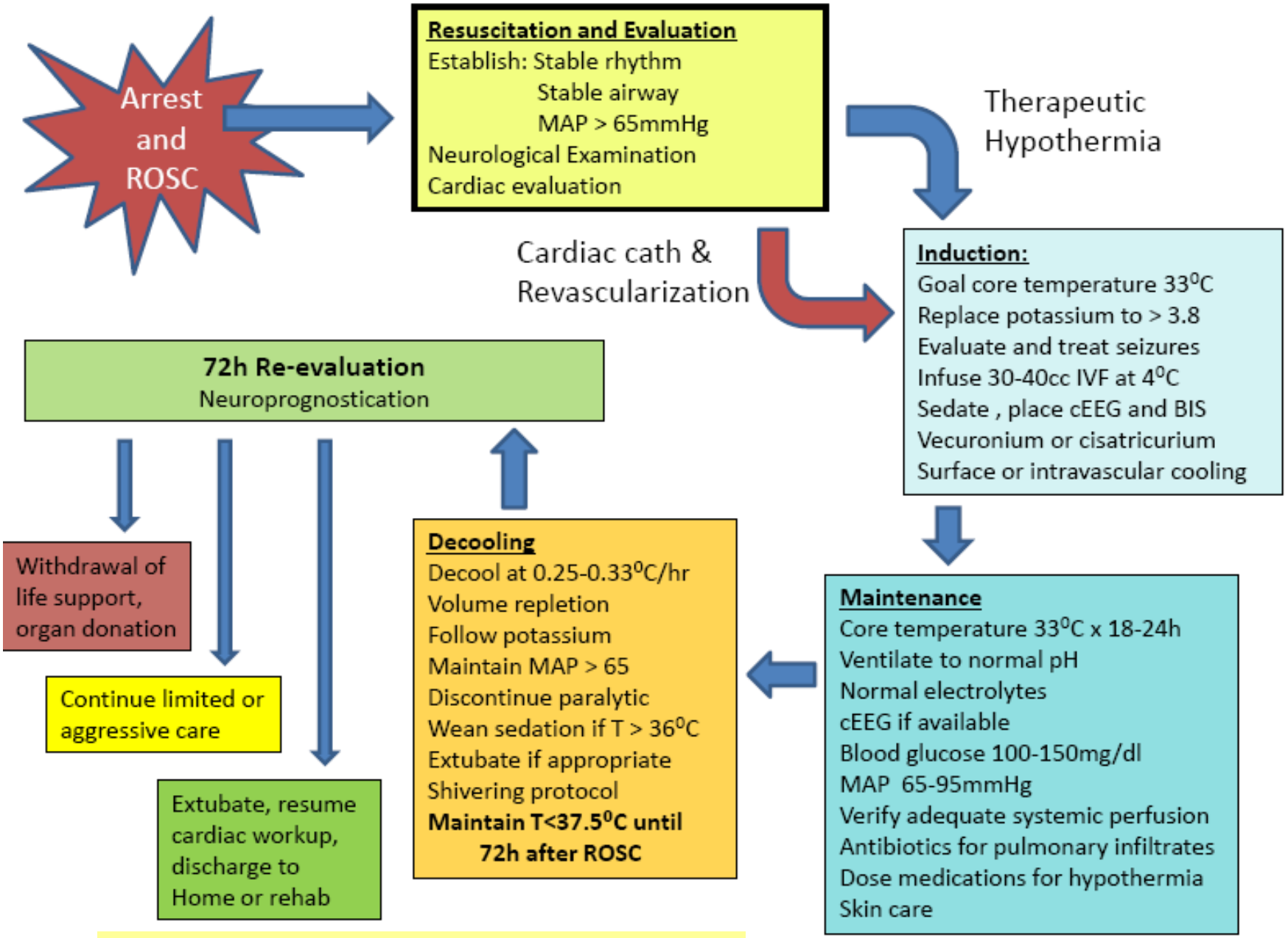
Re-warming
- Should be slow and controlled (0.2 to 0.5°C/h) to avoid:
  (1) Hypoglycemia
  (2) Electrolyte disturbances such as hyperkalemia
  (3) Loss of clinical benefit
- Should be followed by strict maintenance of normothermia since fever may be associated with adverse outcome in post anoxic injury following cardiac arrest

"Maintain Normothermia"

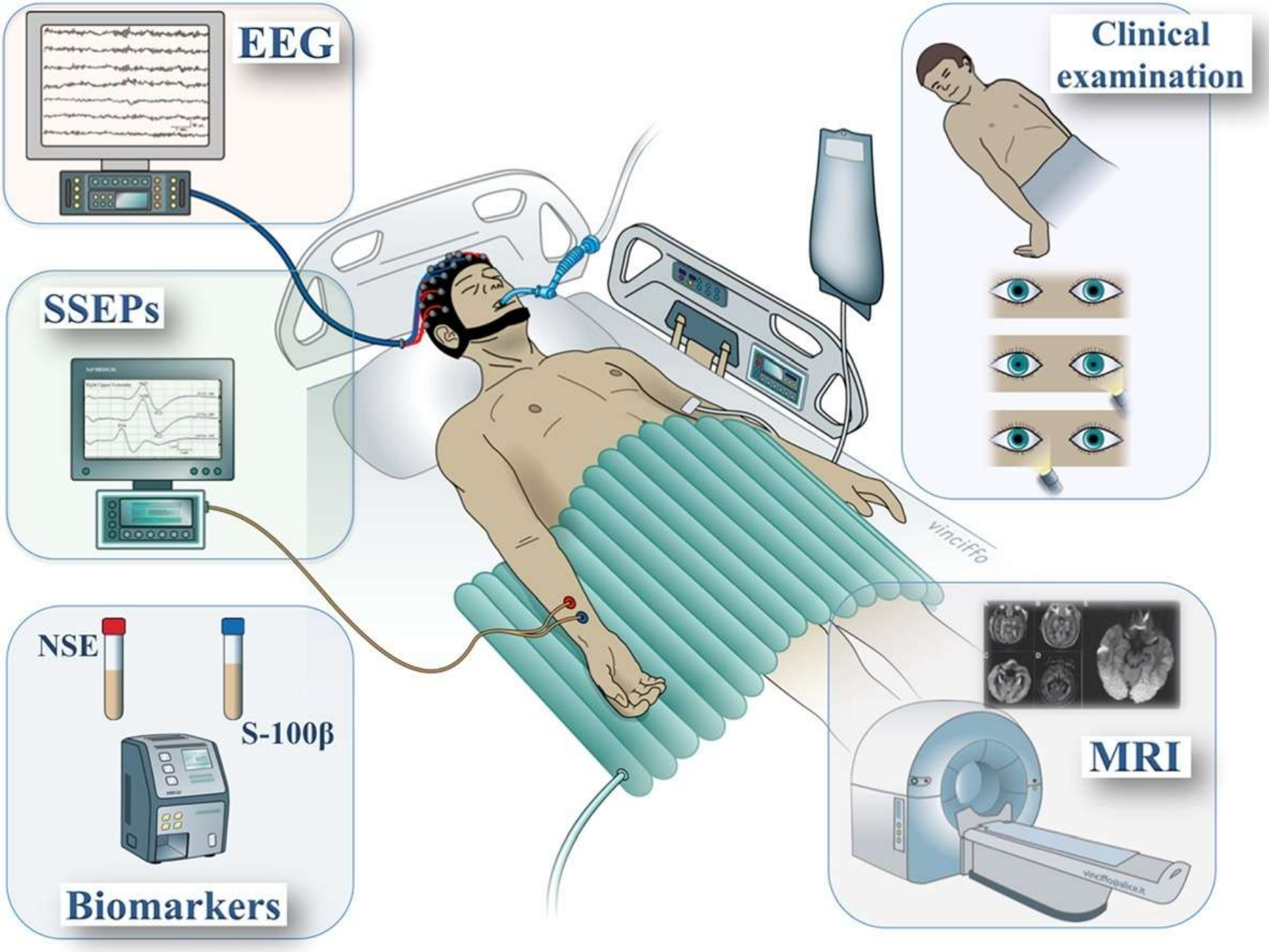
"Cold diuresis"
"Hypovolemia"
"Electrolyte disorders"
"Hyperglycemia"
"Shivering"

"Prevention of infections"
"Continuous EEG: Seizures"

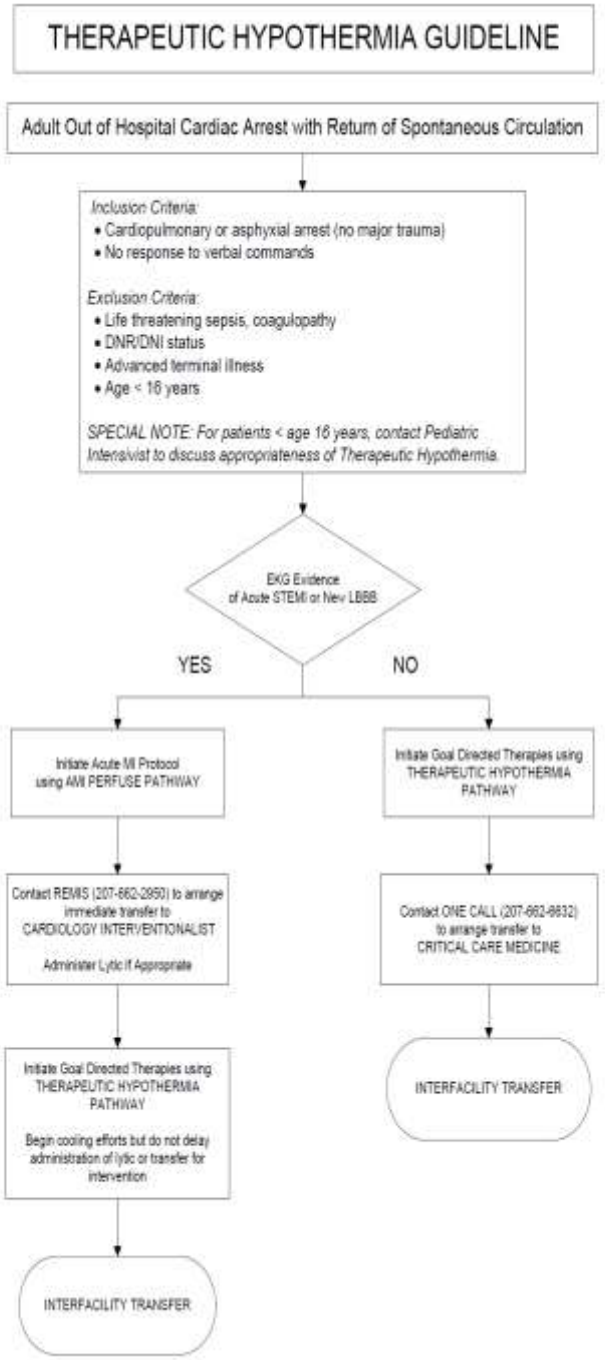
"Hypoglycemia"
"Electrolyte disorders: Hyperkalemia"



Crit Care Med 2009;37 (Suppl):S211-S222.


EEG
Clinical examination
SSEPs
NSE
S-100β
Biomarkers
MRI
vinciffo

MaineHealth CA Guideline



Emergency Department Order Set
Therapeutic Hypothermia for Adult Post Cardiac Arrest

ALLERGIES ☐ **None** ☐ **Yes, Drug/Reaction**_____

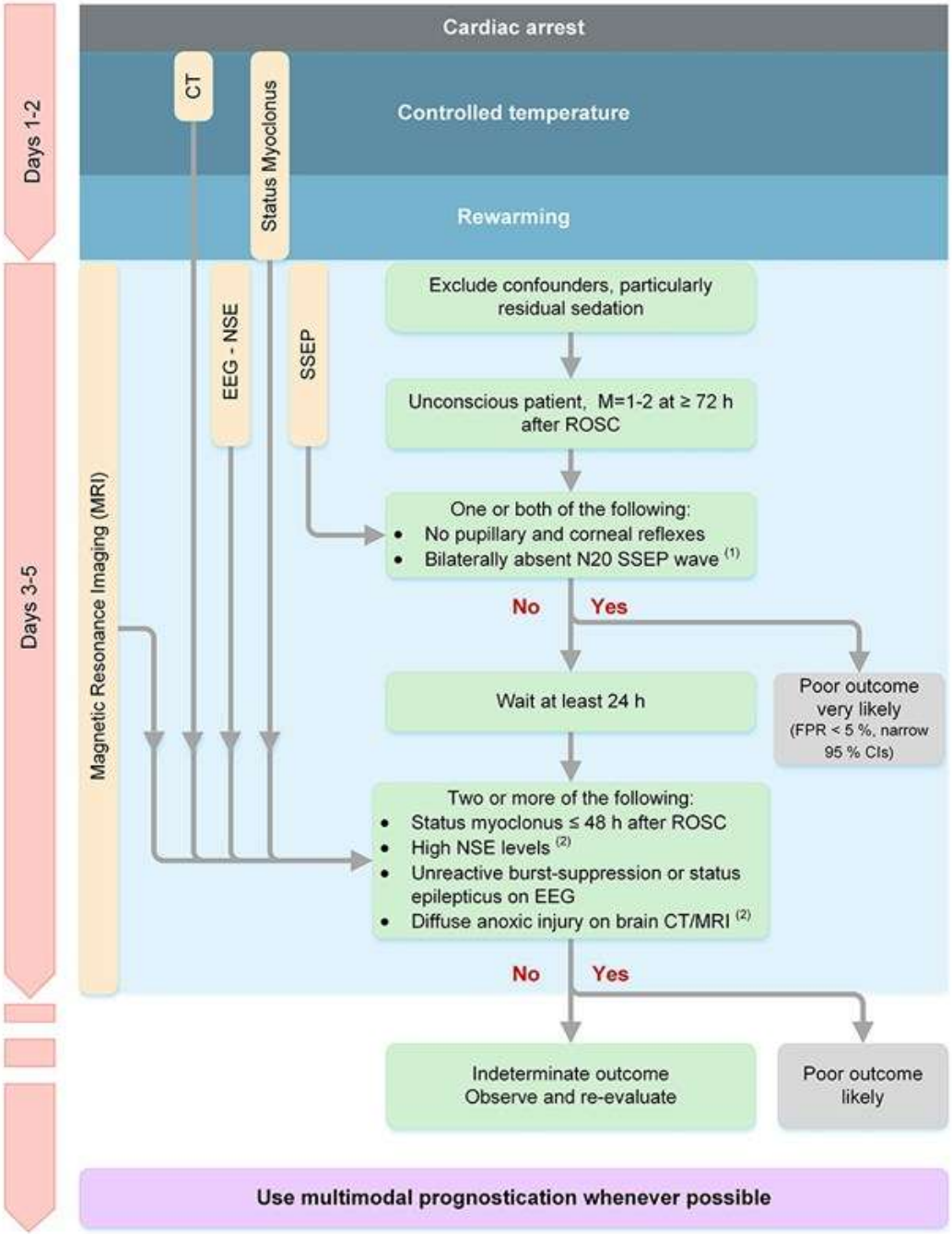
EMERGENCY DEPARTMENT TIMES and INFO TO DOCUMENT

Time of Cardiac Arrest (if unknown, enter time EMS activation and check here ☐)		Total duration of re-arrest(s) after ROSC	
Witnessed arrest Yes/No		Time lytic administered	
Bystander CPR Yes/No		**Initial Core Temperature**	
Time of First CPR		**Time Hypothermia Initiated**	
Initial Rhythm		Time REMIS Called	
Time of Return of Spontaneous Circulation		Time Transport Called	
Time of ED Arrival		Time of Transport Arrival	
Time of 1st EKG		Time of ED Departure	
STEMI Diagnostic EKG Yes/No		**Core Temperature at ED Departure**	

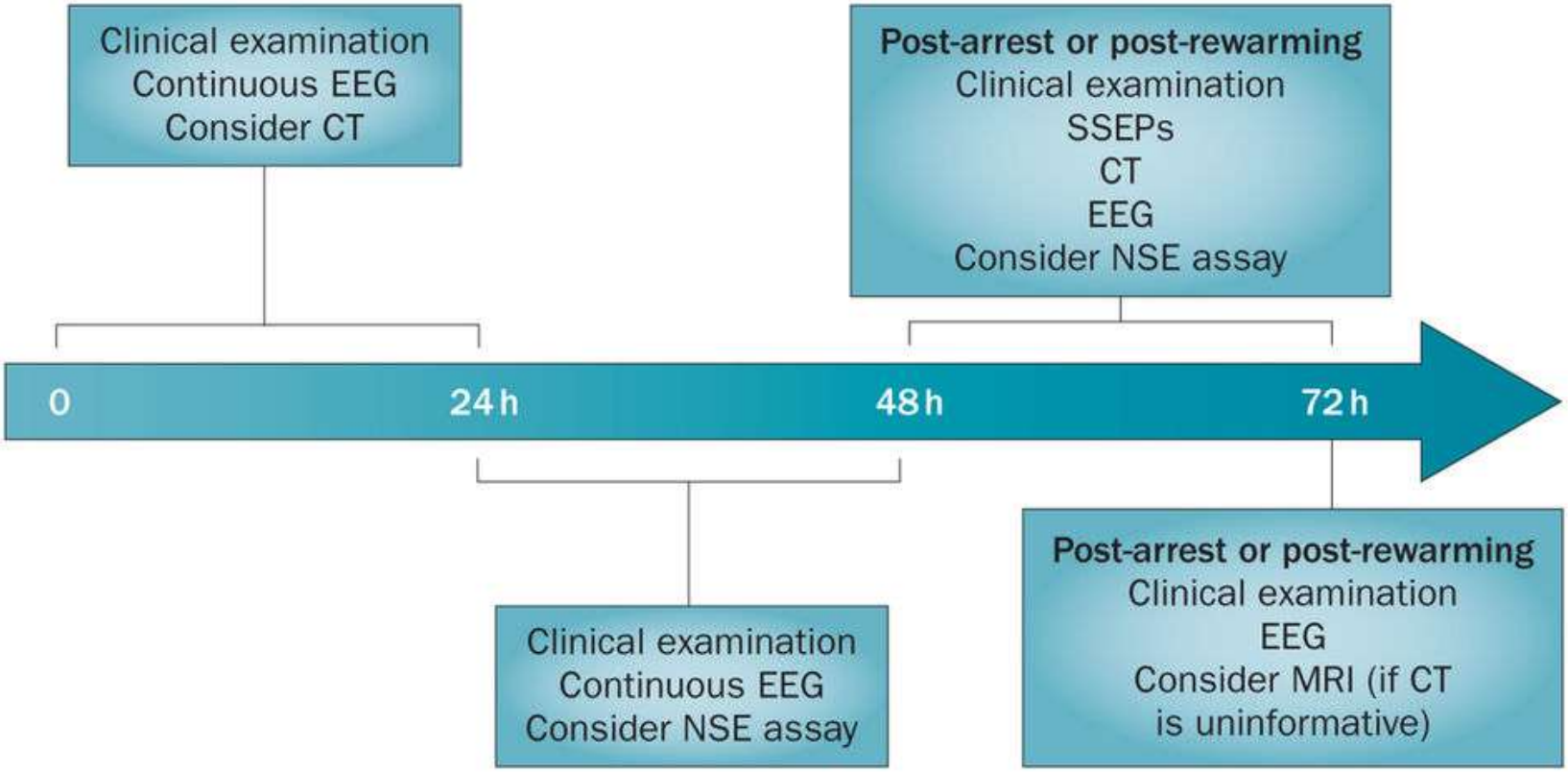
	Insert ✔marks as needed to order tests/treatments not already preselected	Order Noted (Date/Time) (Initial)	
Initial Evaluation			
✔	Vital Signs: BP Pulse RR O_2 Sat Weight (kg)		
✔	Measure Rectal Temperature (record above)		
✔	Continuous Cardiac Monitoring		
✔	Baseline Neurologic Exam (please assess **prior** to paralysis): Following Commands? YES NO Motor Function (circle) Spontaneous purposeful localizes withdraws flexion extension no motor response Symmetrical? YES NO Seizure Activity? YES NO Describe: Pupils mm R mm L React to light? YES NO N/A (atropine) Corneal reflex Present Absent		
Laboratory Tests			
✔	CBC and differential		
✔	Comprehensive Metabolic Profile, Mg^{++}, Phosphorus		
✔	INR/PTT		
✔	Lactate		
✔	CK, CK-MB, Troponin		
✔	ABG		
✔	Urinalysis (Cath)		
	Urine B-HCG in women of childbearing age		
Other Tests			
✔	12 Lead ECG Indication: Post Cardiac Arrest		
✔	Portable AP Chest X-Ray Indication: Intubation, Post OHCA		
	Head CT, non contrast Indication: Post cardiac arrest		
Airway/Breathing Order Set			
✔	Ventilator Settings: CMV mode, target pCO_2 35-45 mm Hg		
✔	FIO_2: **Start at FiO2 0.5** and titrate up as needed to SpO2 greater than 95%		
	PEEP: mg Hg (minimum 5 mm Hg)		
	Rate: breaths/minute (initial 12 breaths/min – higher if severe acidosis)		
	Tidal Volume: ml (recommend 6 to 8 ml/kg of Ideal Body Weight)		
	Place $ETCO_2$ monitor and titrate vent rate to maintain $ETCO_2$ 35-45 mm Hg		
Nursing Procedures			
✔	Expose patient		
	Insert rectal esophageal bladder (circle one) probe for temperature monitoring		
✔	Insert two peripheral IVs, 20 gauge or larger		
✔	Insert Nasogastric or Orogastric tube, intermittent suction		
✔	Insert Foley catheter		
✔	Elevate HOB to 30°		

Prognostication

- prognostication is not reliable until after 72 h
  clinical examination – GCS score, pupillary response to light, corneal reflex, presence of seizures
- neurophysiological studies – somatosensory evoked potentials (SSEPs)
- electroencephalography (EEG)
- biochemical markers neuron-specific enolase (NSE)
- S100B
- imaging studies – brain CT and magnetic resonance imaging (MRI).



(1) At ≥ 24 h after ROSC in patients not treated with targeted temperature
(2) See text for details.


Clinical examination
Continuous EEG
Consider CT
Post-arrest or post-rewarming
Clinical examination
SSEPs
CT
EEG
Consider NSE assay
0
24 h
48 h
72 h
Clinical examination
Continuous EEG
Consider NSE assay
Post-arrest or post-rewarming
Clinical examination
EEG
Consider MRI (if CT
is uninformative)

Summary

- Rapid consideration and early initiation of therapeutic hypothermia
- Aggressive hemodynamic support including PCI when appropriate
- Suppression of shivering and other AEs
- Treatment in an experienced center with appropriate resources

Summary

- Using an aggressive care :
- therapeutic hypothermia,
- hemodynamic support,
- quality ICU care,
- All rhythms: 30-40% GNO
- VT/VT: 50-65% GNO
  - PEA/Asystole 13-25% GNO

AHA Guideline Top Take-Home Message on Post–Cardiac Arrest TTM

- remains important
- Prompt is necessary for all patients who do not follow commands after return of spontaneous circulation to ensure optimal functional and neurological outcome

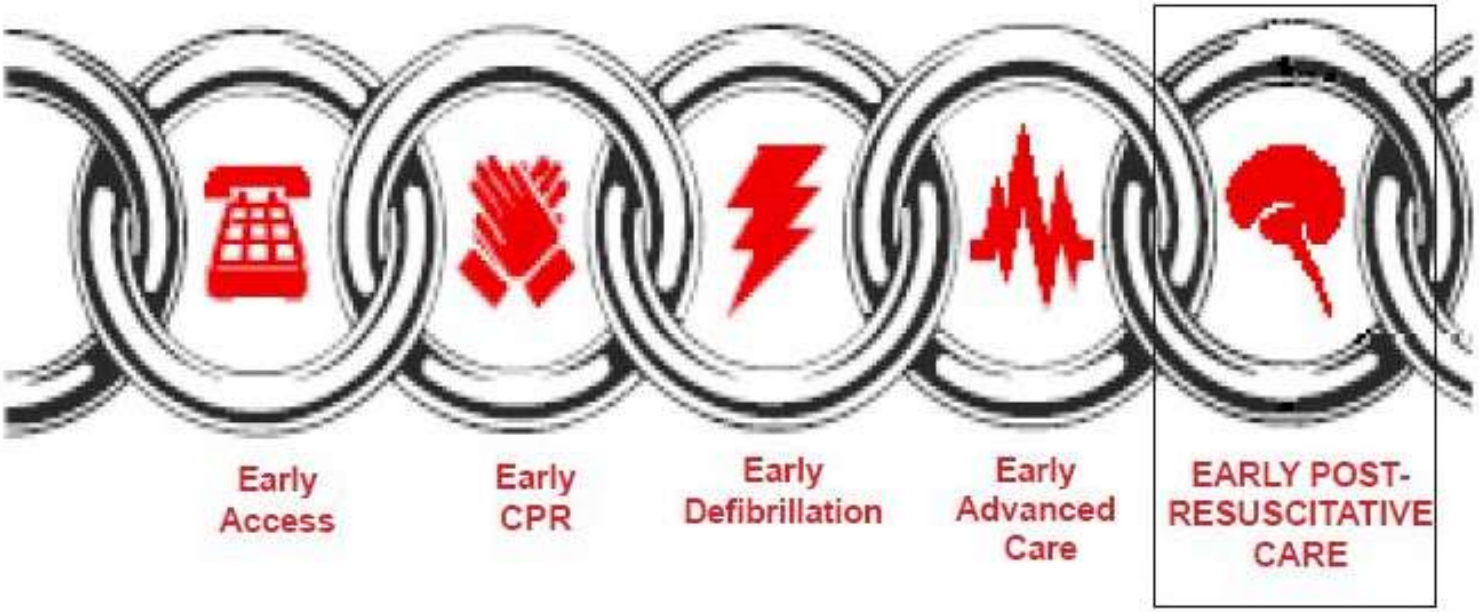
We recommend

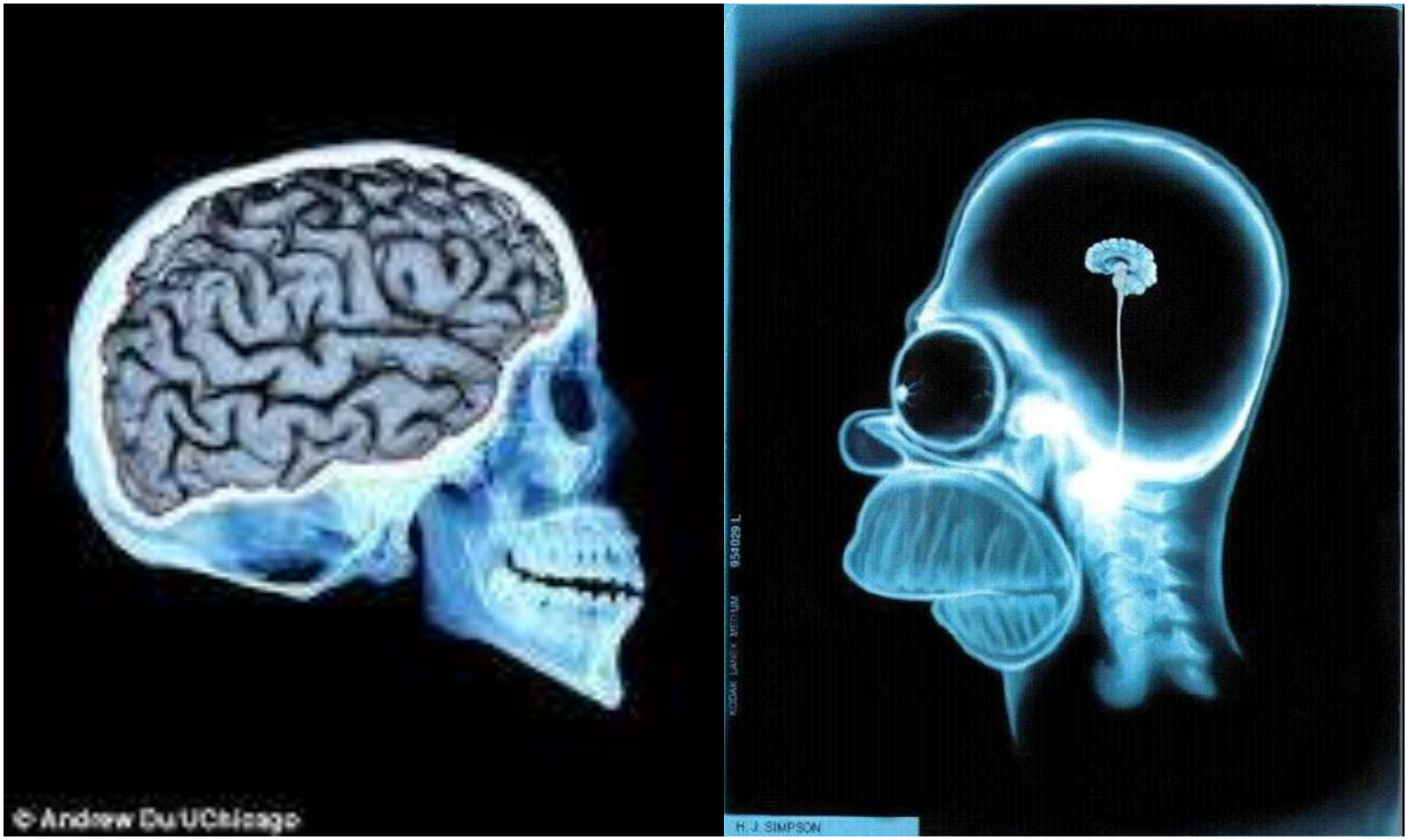
- begin 32-36C for 24 hours by using a cooling device with feedback loop.
- TTM for adult who do not follow commands after ROSC from OHCA with any initial rhythm.
- TTM for adult who do not follow commands after ROSC from IHCA with initial nonshockable rhythm.
- TTM for adult who do not follow commands after ROSC from IHCA with initial shockable rhythm.

Conclusions

- Provide TTM for patients not following commands after cardiac arrest
- Pick a target temperature and stick to it Consider a ‘cushion’ (ie, 35C) to avoid overshooting beyond 36C
- Don’t actively warm patients who are already cooled to within target range
- 4.Once rewarmed, avoid fever unless neurologic recovery has been achieved


Early Access
Early CPR
Early Defibrillation
Early ALS
Early Post Resuscitation Care


Early Access
Early CPR
Early Defibrillation
Early Advanced Care
EARLY POST-RESUSCITATIVE CARE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can expect better OHCA outcomes

Thanks for your attention