Post Cardiac Arrest Management

Ian Pitcher

October 15th 0730-0900

THE UNIVERSITY OF BRITISH COLUMBIA
Continuing Professional Development
Faculty of Medicine

Land Acknowledgement

We acknowledge that we work on the traditional, ancestral and unceded territory of the Skwxwú7mesh (Squamish), xʷməθkwəy̓əm (Musqueam), and Sə̓lílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.

UBC CPD
Medicine
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DEVELOPMENT

Presenter Disclosures

- None

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Learning Objectives

- Review current evidence and recommendations for post cardiac arrest temperature management
- Review evidence and pathways for neuroprognostication post cardiac arrest
- Review when transfer to other centers is indicated

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Case

65M is admitted with an OHCA

- He had a witnessed arrest while walking his dog with immediate bystander CPR
- He initially had a shockable rhythm from the EHS reports and was intubated in the field
- His ECG in the ED does not show a STEMI

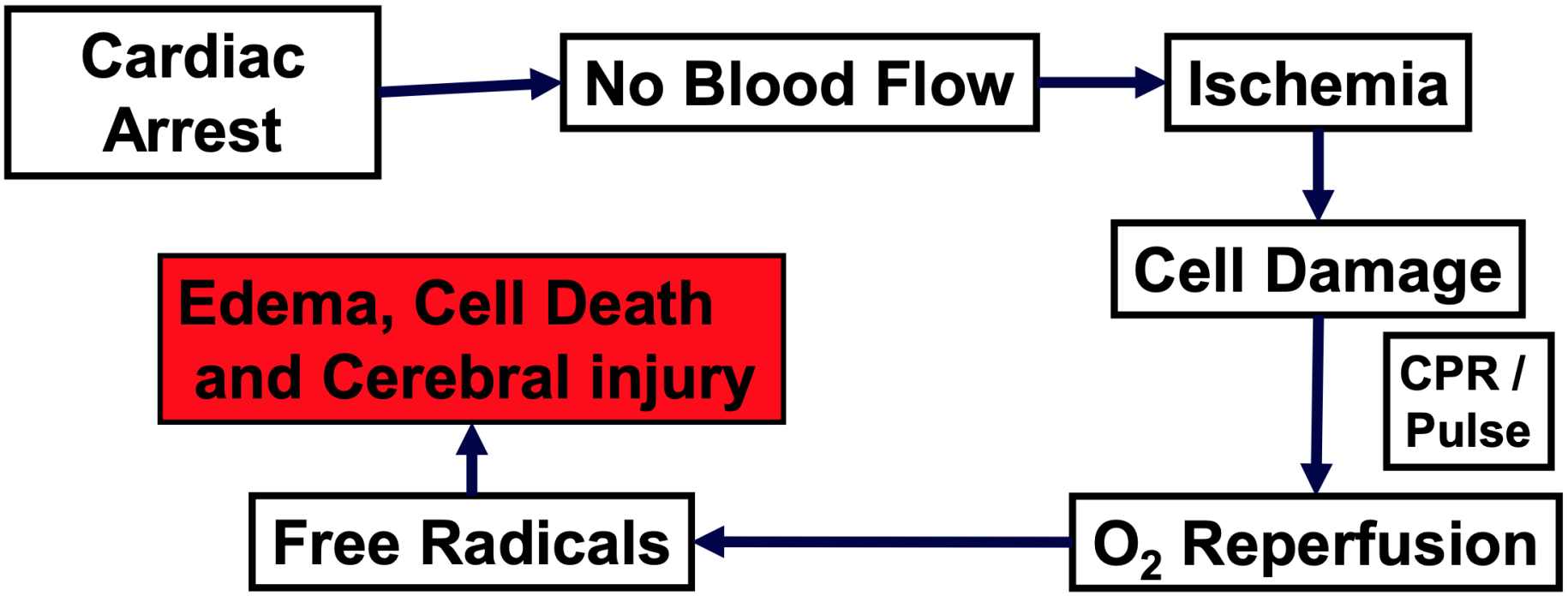
Case

- Should he be cooled?
- At what temperature target?

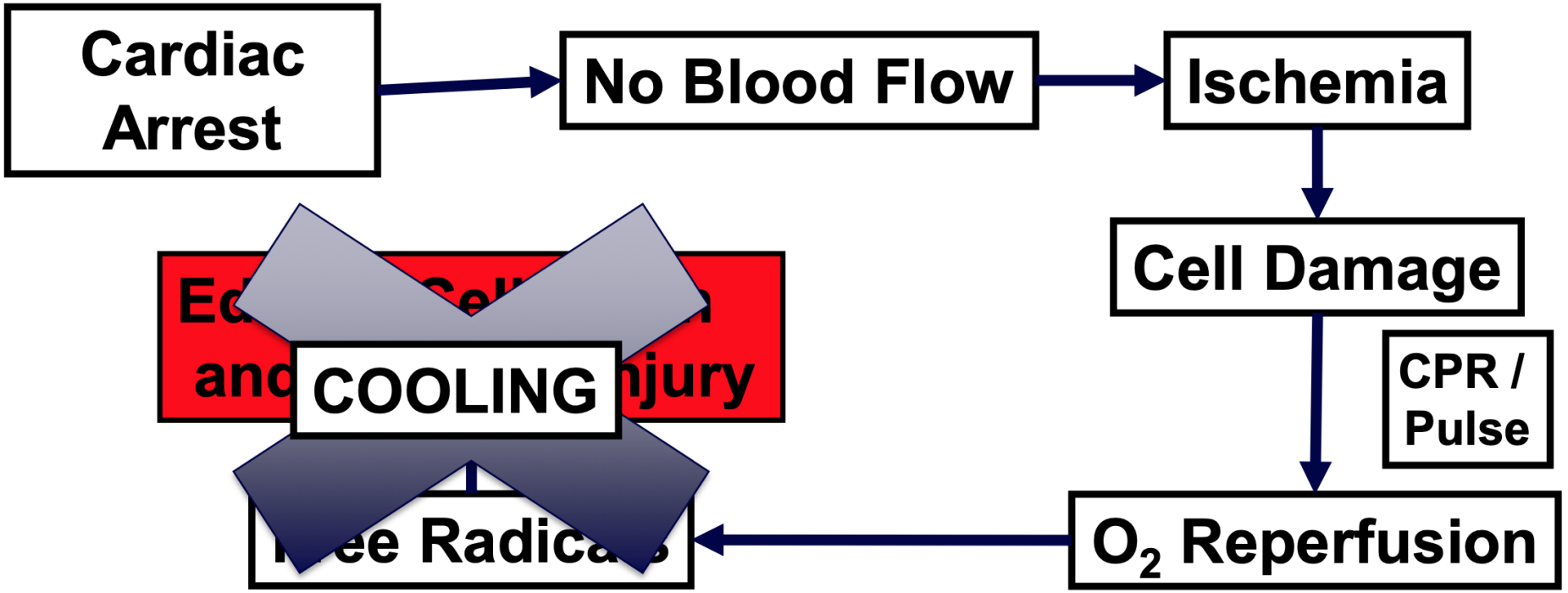
Background

- There are more than 300,000 out-of-hospital cardiac arrests per year in Europe alone
- 30-55% survive to discharge
- Hypothermia was the only intervention to show an improvement in outcomes

Metabolic Chain of Events After Cardiac Arrest



Metabolic Chain of Events After Cardiac Arrest



Bernard et al. Trial

- Randomized* 84 patients with an initial rhythm of VF
  - Patients were randomized by the day of the month
- 7 were excluded → 77 analyzed
- Non-blinded
- It wasn't documented how many patients were screened to find the 84 patients

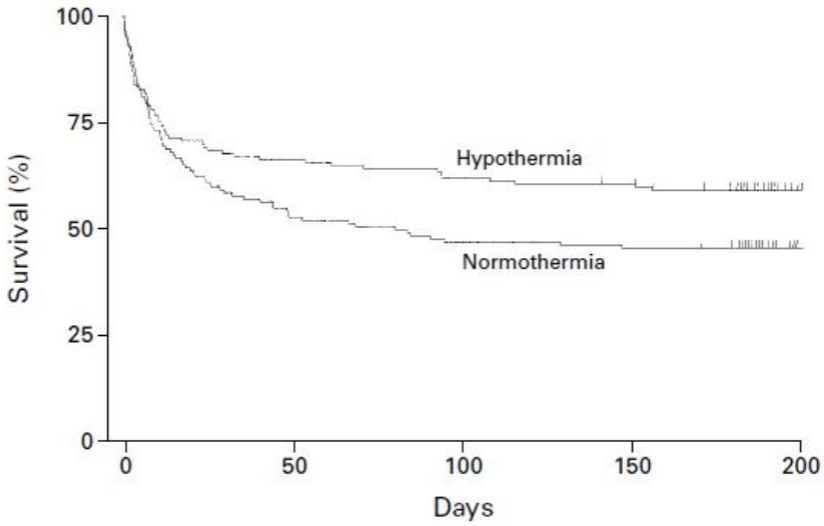
Bernard et al. trial

- Patients were cooled to 33 degrees C for 12 hours
- Primary outcome of good neurologic outcome in patients sent home or to rehab occurred in 49% of the hypothermia and 26% of normothermia ($p = 0.046$)
- Mortality was not statistically different (51% vs 68% $p = 0.16$)

Hypothermia After Cardiac Arrest Trial (HACA)

- 275 OHCA patients with a shockable rhythm and presumed cardiac arrest were randomized to cooling at 32-34 degrees C for 24 hours followed by 8 hours of passive rewarming

HACA



No. at Risk					
Hypothermia	137	92	86	83	11
Normothermia	138	74	66	64	9

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

- Primary outcome: good neurologic outcome at 6 months
  - 55% in hypothermia vs 39% of normothermia
  - P = 0.009, RR 1.40, CI 1.08-1.81
- Six month mortality was also improved in the hypothermia group (41% vs 55%, p = 0.02)

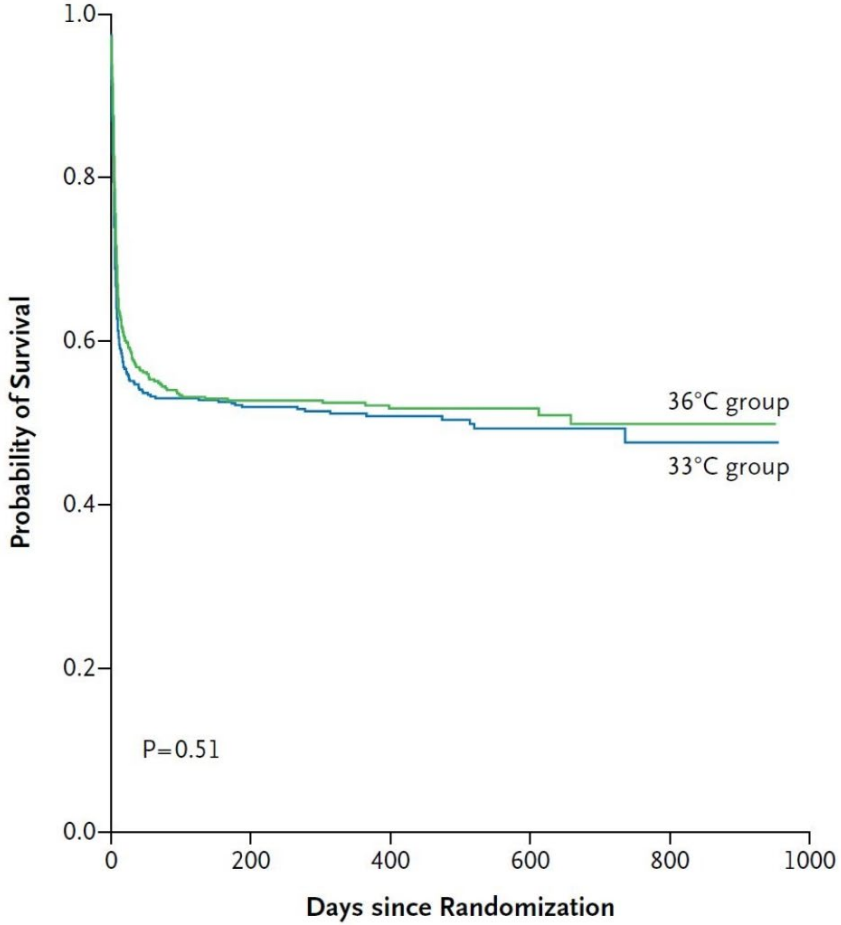
Limitations

- Unblinded to the treating physicians
  - Many deaths are from the withdrawal of care. Did delay of the withdraw of care lead to more survival in the hypothermia group?
- Hypothermic patients require more clinical attention → did they get better overall intensive care?
- Many patients in the control group developed fever
  - Is it just the fever that's bad?
- Both were very small trials

TTM Trial

- Published in 2013
- Multicentre RCT involving 36 ICUs in Europe and Australia
- Enrolled 950 patients with OHCA regardless of presenting rhythm (80% had a shockable rhythm)

TTM Trial



No. at Risk					
33°C group	473	230	151	64	15
36°C group	466	235	144	68	12

- No difference in the primary outcome of death (50% vs 48% p = 0.51)
- No difference in neurologic outcomes

Interpretations

1. Is there a difference in patients with shockable and non-shockable outcomes (80% shockable in TTM)
2. Is there a benefit to cooling or does fever just need to be avoided
   - Normothermia group not allowed to be febrile in TTM compared to both 2002 trials

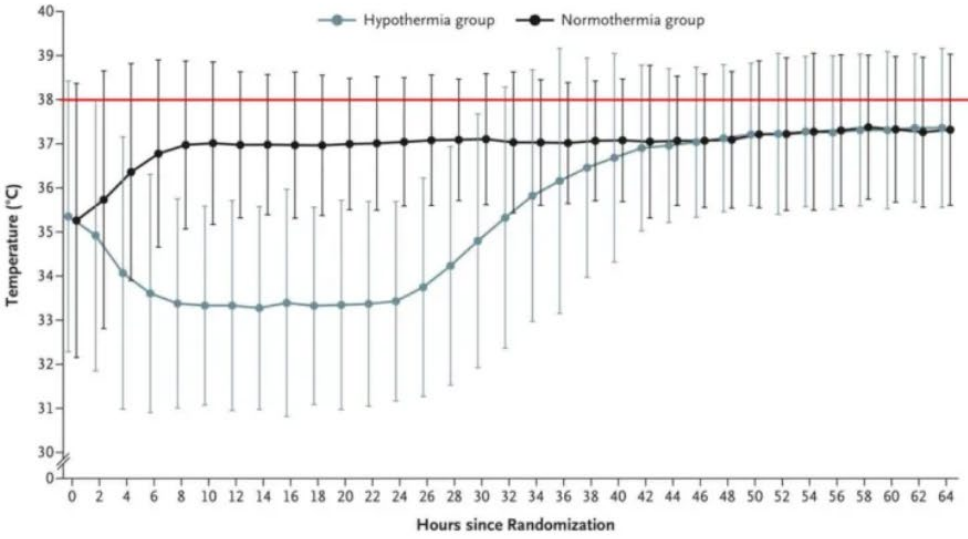
HYPERION trial

- Published in 2019 in NEJM
- Patients – 584 total
  - Included patients with an out of hospital of in-hospital cardiac arrest with a non-shockable rhythm
  - Patients were excluded if they had more than 10 minutes without CPR or over 60 minutes of CPR total
- Intervention:
  - 33 vs 36.5-37.5C

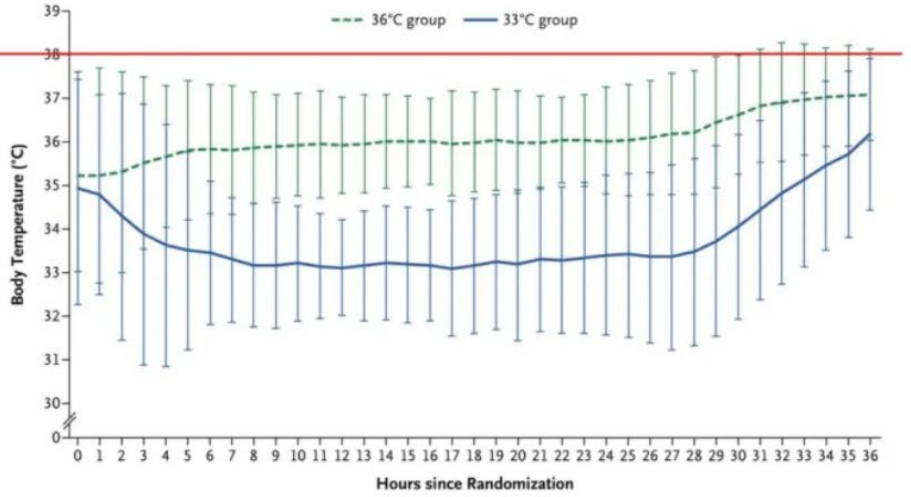
HYPERION

- Primary outcome of a favourable neurologic outcome was positive at day 90 (10.2% vs 5.7, p= 0.047)
  - Fragility index 1
- Criticized for the fragility of the results and the poor precision of temperature control in the 37C group

HYPERION trial



TTM trial



TTM-2

- 1850 OHCA patients were randomized to either targeted hypothermia at 33 degrees or targeted normothermia with early treatment of fever (T>37.8 degrees) for 28 hours
- Avoidance of fever was maintained for 72 hours after randomization

Table 1 cont.

Characteristic	Hypothermia (N=930)	Normothermia (N=931)
First monitored rhythm — no. (%)		
Shockable rhythm	671 (72)	700 (75)
Ventricular fibrillation	576 (62)	585 (63)
Nonperfusing ventricular tachycardia	31 (3)	29 (3)
ROSC after bystander-initiated defibrillation	24 (3)	41 (4)
Unknown rhythm, shock administered	40 (4)	45 (5)
Nonshockable rhythm	259 (28)	231 (25)
Pulseless electrical activity	117 (13)	113 (12)
Asystole	124 (13)	100 (11)
Unknown rhythm, no shock administered	18 (2)	18 (2)
Median time from cardiac arrest to sustained ROSC (IQR) — min§	25 (16–40)	25 (17–40)
Median time from cardiac arrest to randomization — min (IQR)	136 (103–170)	133 (99–173)
Clinical characteristics on admission		
Tympanic temperature — °C¶	35.3±1.1	35.4±1.1
FOUR motor score‖	0	0
Bilateral corneal reflexes present — no./total no. (%)	168/511 (33)	194/537 (36)
Bilateral pupillary reflexes present — no./total no. (%)	535/761 (70)	529/776 (68)
Arterial pH**	7.2±0.2	7.2±0.2
Arterial lactate level — mmol/liter††	5.9±4.4	5.8±4.2
Shock — no. (%)‡‡	261 (28)	275 (30)
ST-segment elevation myocardial infarction — no./total no. (%)	379/918 (41)	370/921 (40)

The NEW ENGLAND JOURNAL of MEDICINE

Hypothermia vs. Normothermia after Out-of-Hospital Cardiac Arrest

OPEN-LABEL TRIAL WITH BLINDED OUTCOME ASSESSMENT

1850
Comatose adults after out-of-hospital cardiac arrest

	Hypothermia (target body temperature, 33°C) N=925	Normothermia (target body temperature, ≤37.5°C) N=925
Death from any cause at 6 mo	50%	48%
	RR, 1.04; 95% CI, 0.94 to 1.14; P=0.37	
Modified Rankin scale score ≥4 at 6 mo	55%	55%
	RR, 1.00; 95% CI, 0.92 to 1.09	
Arrhythmia with hemodynamic compromise	24%	17%

Hypothermia did not lead to a lower 6-mo incidence of death than normothermia.

J. Dankiewicz et al. 10.1056/NEJMoa2100591

Authors Conclusions

- Reasons for the contrast with previous trials include
  - Improvement in standard critical care practices
  - Lower risk of bias in the current trial
  - Lower risk of random error given the larger sample size (5x previous trials)

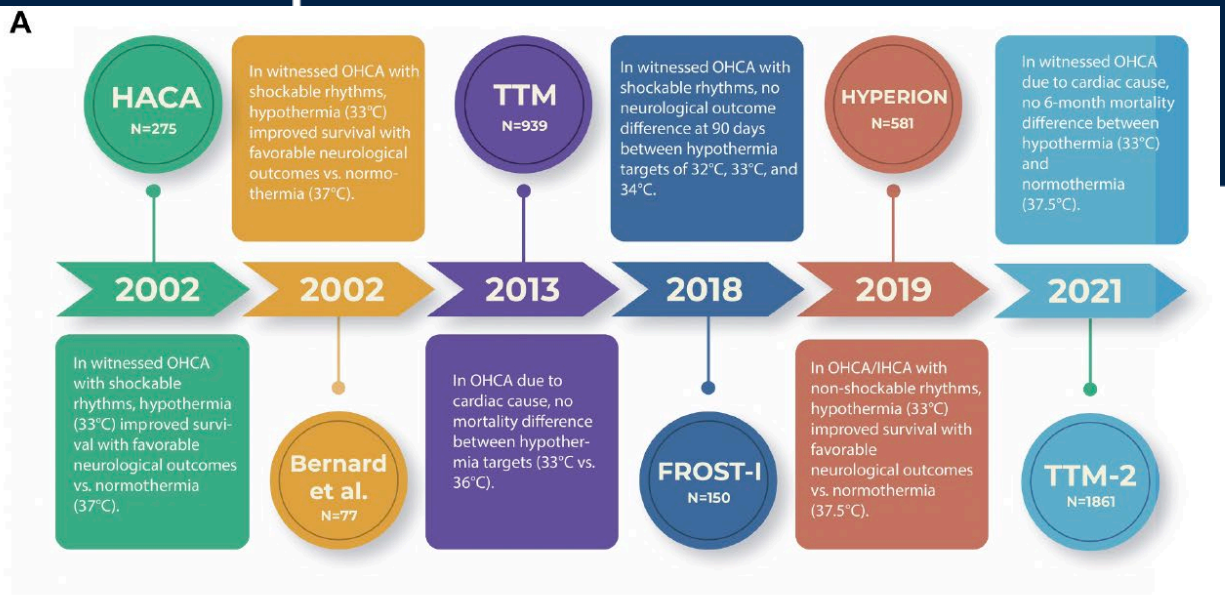
What is the approach to cooling now?

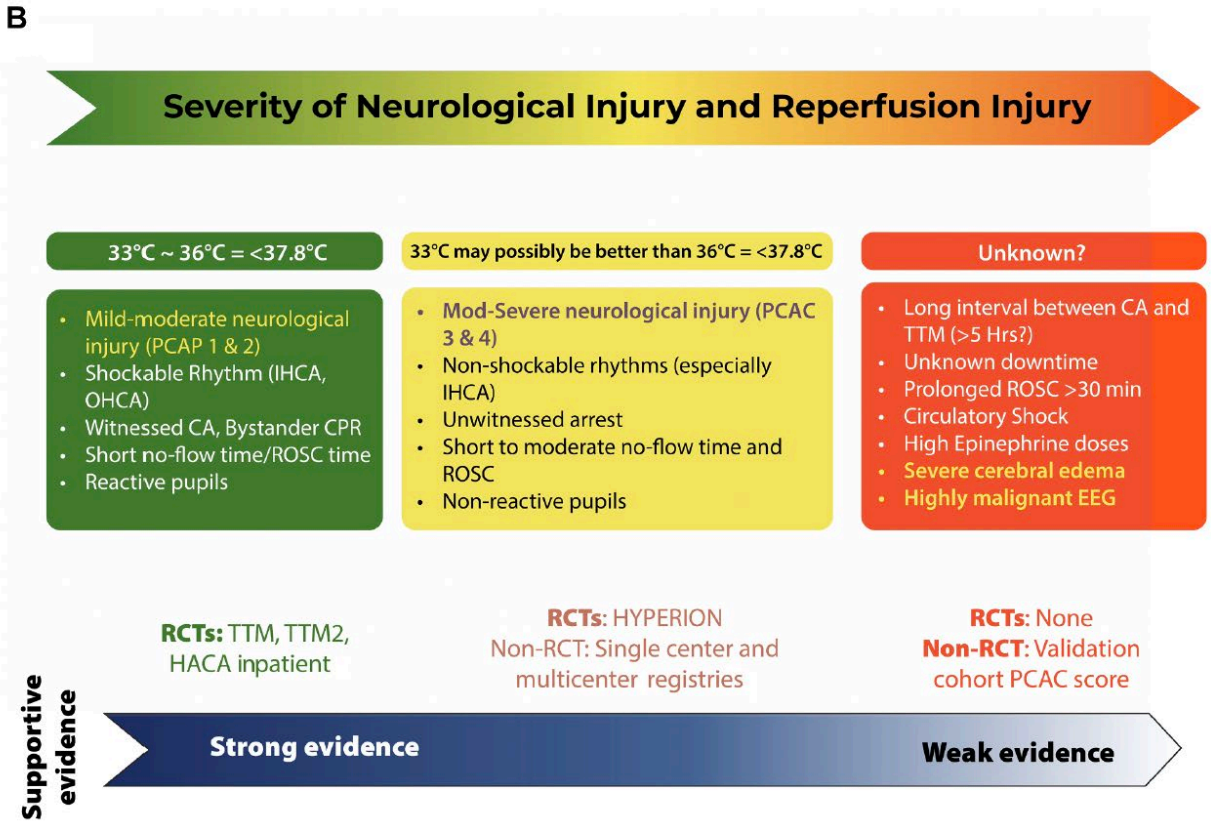
Table 2 ERC-ESICM Recommendations for temperature control after cardiac arrest in adults

GOOD PRACTICE	We **recommend** continuous monitoring of core temperature in patients who remain comatose after ROSC from cardiac arrest.
LOW	We **recommend** actively preventing fever (defined as a temperature > 37.7°C) in post-cardiac arrest patients who remain comatose.
GOOD PRACTICE	We **recommend** actively preventing fever for at least 72 hours in post-cardiac arrest patients who remain comatose.
GOOD PRACTICE	Temperature control can be achieved by exposing the patient, using anti-pyretic drugs, or if this is insufficient, by using a cooling device with a target temperature of 37.5°C.
GOOD PRACTICE	There is currently insufficient evidence to recommend for or against temperature control at 32-36°C in sub-populations of cardiac arrest patients or using early cooling, and future research may help elucidate this. We **recommend not** actively rewarming comatose patients with mild hypothermia after ROSC to achieve normothermia.
MODERATE	We **recommend not** using prehospital cooling with rapid infusion of large volumes of cold IV fluid immediately after ROSC.

AHA Guidelines

Performance of Temperature Control		
COR	**LOE**	**Recommendations**
1	B-R	1. We recommend selecting and maintaining a constant temperature between 32°C and 37.5°C during postarrest temperature control.
1	B-NR	2. We recommend hospitals develop protocols for postarrest temperature control.
2a	B-NR	3. It is reasonable that temperature control be maintained for at least 24 h after achieving target temperature.
2b	B-NR	4. There is insufficient evidence to recommend a specific therapeutic temperature for different subgroups of cardiac arrest patients.
2b	C-LD	5. It may be reasonable to actively prevent fever in patients unresponsive to verbal commands after initial temperature control.
2b	C-EO	6. Patients with spontaneous hypothermia after ROSC unresponsive to verbal commands should not routinely be actively or passively rewarmed faster than 0.5°C per hour.
2b	B-R	7. The benefit of strategies other than rapid infusion of cold intravenous fluids for prehospital cooling is unclear.
3: No Benefit	B-R	8. We do not recommend the routine use of rapid infusion of cold intravenous fluids for prehospital cooling of patients after ROSC.





Mark et al JACC 2025

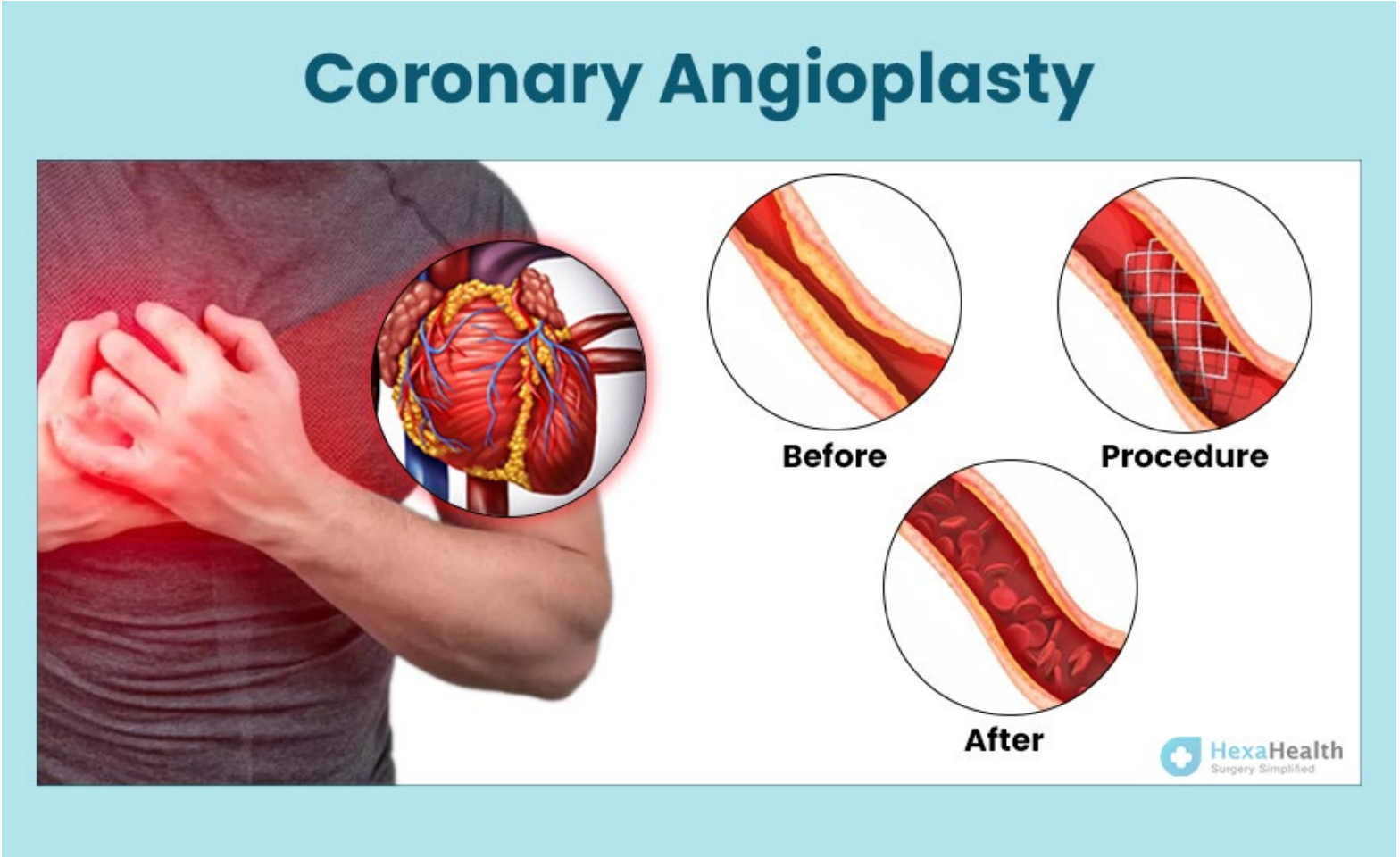
My approach

- If the primary arrest is thought to be of cardiac etiology (ie CCU patient) then I target a temperature less than 37.5.
- If there has been difficulty achieving the target temperature I will set target temp to < 37 to avoid fevers
- In patient with non-cardiac etiology of arrest I will follow institutional practice patterns but will often target less than 37.5

Other future developments?

- Duration of sedation
- Does management of fever change outcomes?

Coronary Angiography Post Arrest?



COACT (2019)

- Immediate versus delayed cath and PCI in 522 OHCA patients with a shockable rhythm without ST elevation on post-ROSC ECG.
- The primary outcome of 90-day survival was not significantly different between the two groups (64.5% in immediate and 67.2% in the delayed cath group; p = 0.51).
- There was no difference in the secondary outcomes including survival with good cerebral function, recurrence of VT requiring defibrillation, markers of shock, duration of mechanical ventilation or inotropic support, and TTM.
- Immediate strategy affected some aspects of the care including later target temperature achievement, less use of oral antiplatelets, and more use of glycoprotein IIb/IIIa inhibitors compared with the delayed cath group
- One-year follow-up of COACT trial showed similar results with no significant difference in survival between the immediate group (61.4%) and delayed group (64.0%).

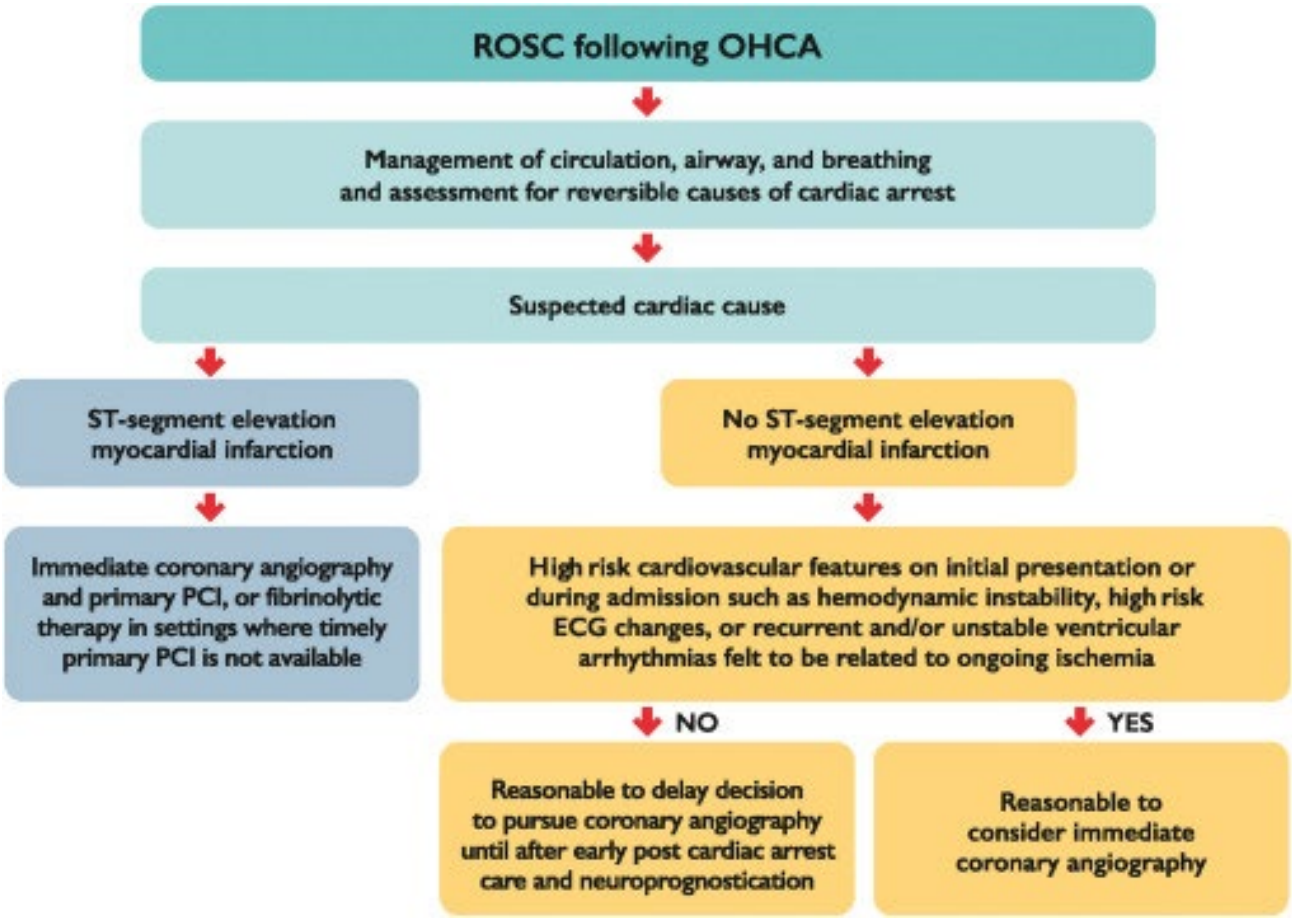
TOMAHAWK (2021)

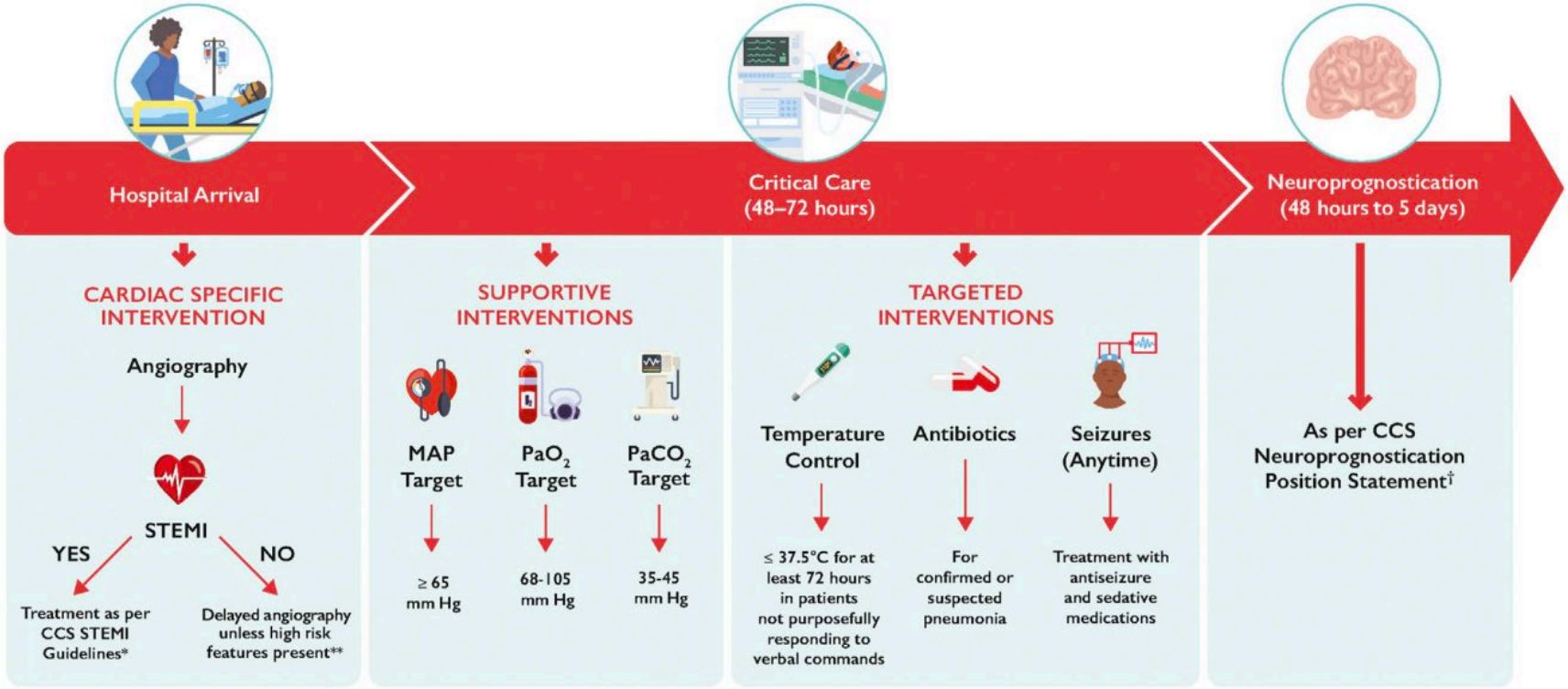
- 554 patients with successfully resuscitated out-of-hospital cardiac arrest of possible coronary origin (both shockable and non-shockable arrest rhythms were enrolled) randomized to undergo either immediate coronary angiography or initial intensive care assessment with delayed or selective angiography. All the patients had no evidence of ST-segment elevation on post resuscitation electrocardiography.

- At 30 days, 143 of 265 patients (54.0%) in the immediate-angiography group and 122 of 265 patients (46.0%) in the delayed-angiography group had died (hazard ratio, 1.28; 95% confidence interval [CI], 1.00 to 1.63; P=0.06).
- The composite of death or severe neurologic deficit occurred more frequently in the immediate-angiography group (in 164 of 255 patients [64.3%]) than in the delayed-angiography group (in 138 of 248 patients [55.6%]), for a relative risk of 1.16 (95% CI, 1.00 to 1.34).
- Coronary angiography was performed in 95.5% of patients in the immediate-angiography group and in 62.2% of those in the delayed-angiography group.

PERCUTANEOUS CORONARY INTERVENTION AFTER CARDIAC ARREST

Percutaneous Coronary Intervention After Cardiac Arrest		
COR	**LOE**	**Recommendation**
1	B-NR	1. Coronary angiography should be performed emergently for all cardiac arrest patients with suspected cardiac cause of arrest and ST-segment elevation on electrocardiogram.
2a	B-NR	2. Emergent coronary angiography is reasonable for selected adult patients without ST-elevation on electrocardiogram but with elevated risk of significant coronary artery disease where revascularization may provide benefit, such as those with shock, electrical instability, signs of significant ongoing myocardial damage, or ongoing ischemia.
2a	C-LD	3. Independent of a patient's neurologic status, coronary angiography is reasonable in all post–cardiac arrest patients for whom coronary angiography is otherwise indicated.
3: No Benefit	B-R	4. Emergent coronary angiography is not recommended over a delayed or selective strategy in patients with ROSC after cardiac arrest in the absence of ST-segment elevation, shock, electrical instability, signs of significant myocardial damage, and ongoing ischemia.


ROSC following OHCA
Management of circulation, airway, and breathing and assessment for reversible causes of cardiac arrest
Suspected cardiac cause
ST-segment elevation myocardial infarction
Immediate coronary angiography and primary PCI, or fibrinolytic therapy in settings where timely primary PCI is not available
No ST-segment elevation myocardial infarction
High risk cardiovascular features on initial presentation or during admission such as hemodynamic instability, high risk ECG changes, or recurrent and/or unstable ventricular arrhythmias felt to be related to ongoing ischemia
NO
YES
Reasonable to delay decision to pursue coronary angiography until after early post cardiac arrest care and neuroprognostication
Reasonable to consider immediate coronary angiography



* Wong et al. Can J Cardiol 2019;35:107-132.
† Fordyce et al. Can J Cardiol 2023;39:366-380.
** High risk features include hemodynamic instability, high risk ischemic ECG changes, or recurrent and/or unstable ventricular arrhythmias.

Neuroprognostication

- The most common cause of death post care arrest is withdrawal of care
- Difficult balance of supporting patient's recovery, continuing care on those who may recover and not prolonging futile care in others

Goals of care

- Outline early what the patient would want in regards to quality of life. This is important for the family to begin to discuss and may be important in later stages for medical legal reasons.

What are our predictors of a poor neurologic outcome?

Table 3 – Patient and CPR factors affecting outcome from OHCA. Adapted from Kandala 2017.[46] AED automated external defibrillation; CPR cardiopulmonary resuscitation.

Resuscitation Attempt and Outcomes in Patients With Asystole Out-of-Hospital Cardiac Arrest

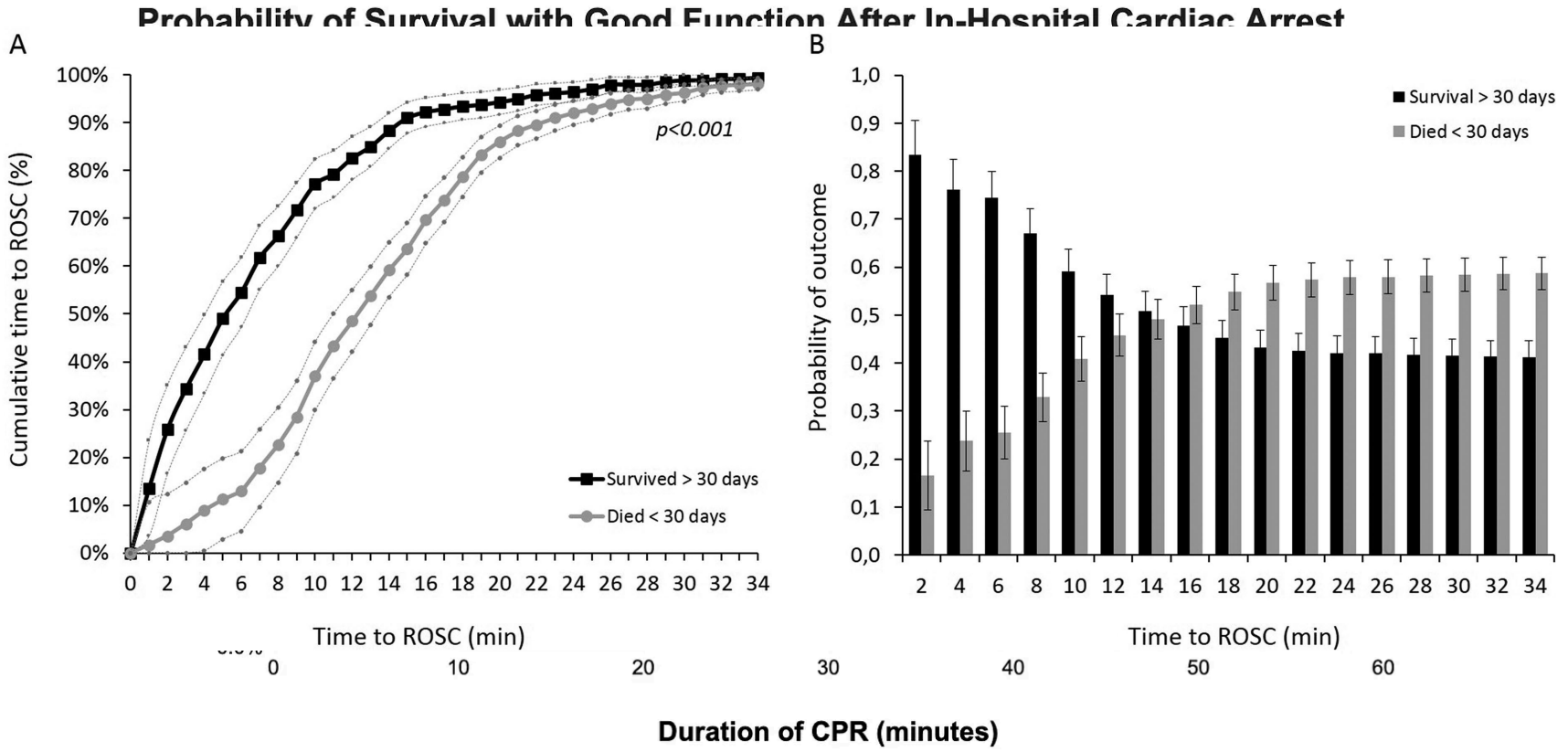
Junki Ishii, MD[1]; Mitsuaki Nishikimi, MD, PhD[1]; Kazuya Kikutani, MD, PhD[1] ; et al

» Author Affiliations | Article Information

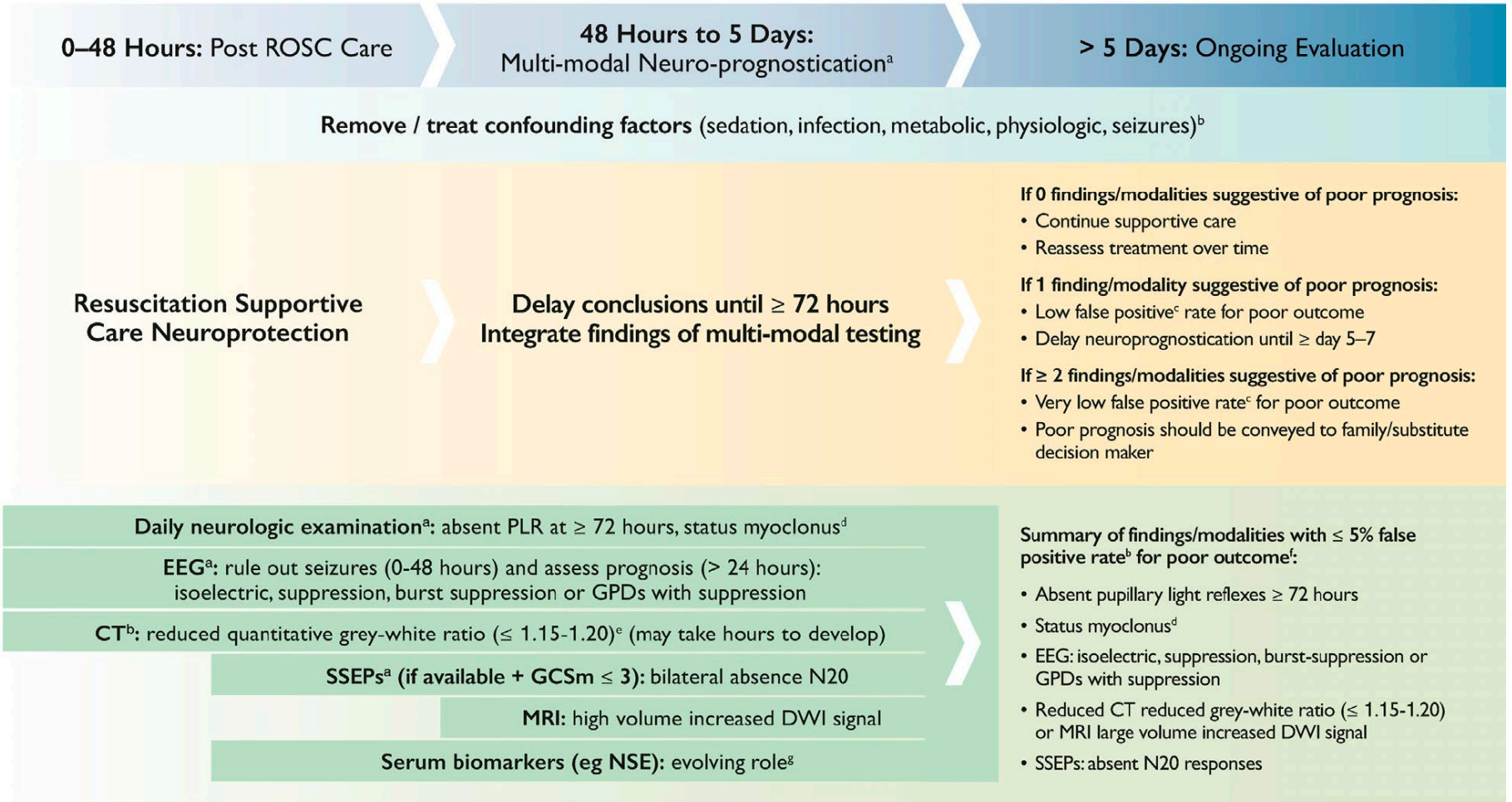
Cardiopulmonary resuscitation

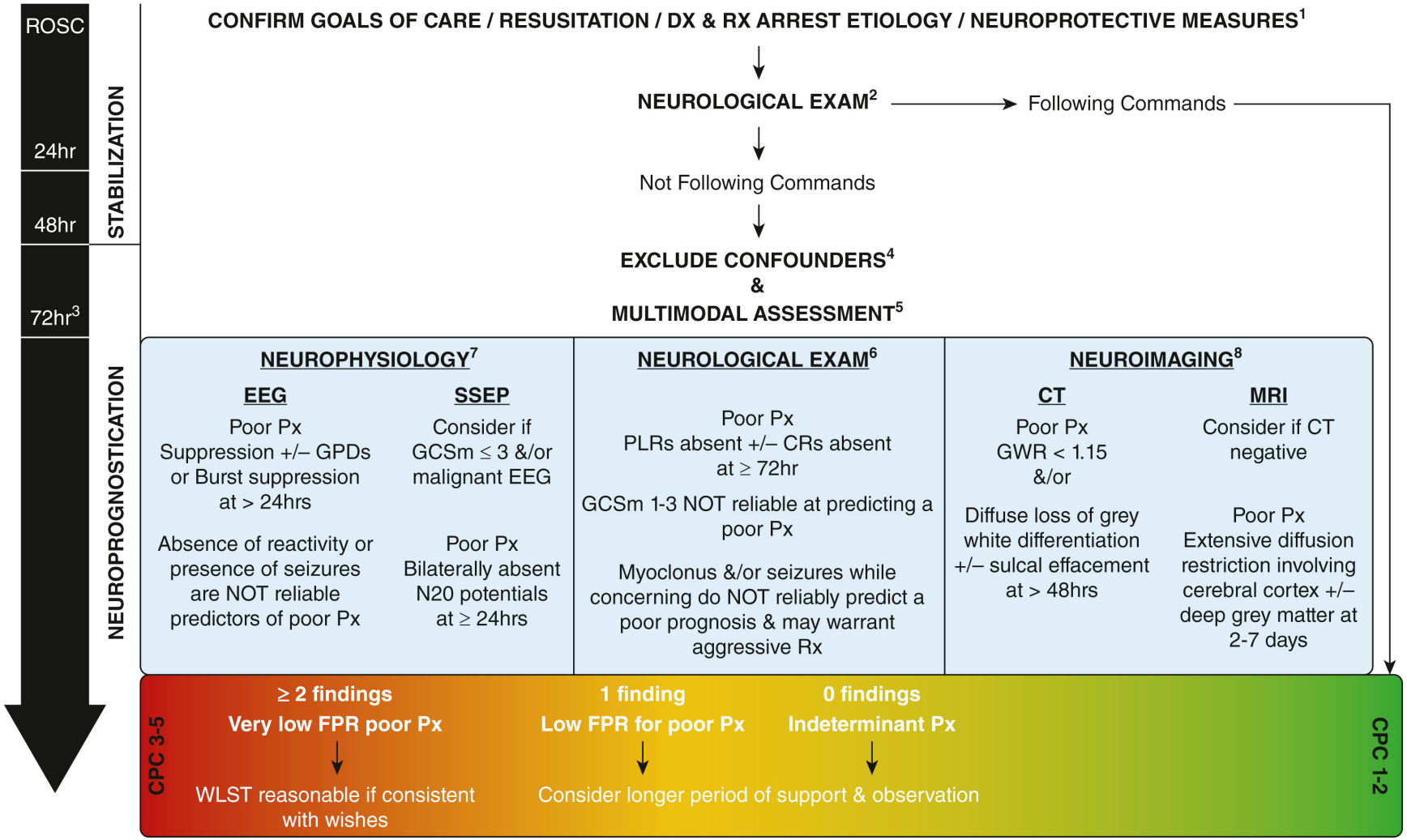
- Location (private vs. public)
- Witnessed vs. unwitnessed cardiac arrest
- Bystander CPR
- Type of bystander CPR (compression only vs. standard)
- First cardiac arrest rhythm
- Use of AED by bystander
- Time to return of spontaneous circulation

- Duration


Probability of Survival with Good Function After In-Hospital Cardiac Arrest
A
Cumulative time to ROSC (%)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
p<0.001
Survived > 30 days
Died < 30 days
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34
Time to ROSC (min)
B
Probability of outcome
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
Survival > 30 days
Died < 30 days
2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34
Time to ROSC (min)
0 10 20 30 40 50 60
Duration of CPR (minutes)

Fordyce et al.
Neuroprognostication Post Cardiac Arrest





Kromm et al CHEST 2024

Neurologic exam

- Remains foundational for neuroprognostication
- Unreliable in the first 24hrs – lack of brainstem reflexes not definitive of a poor outcome

Neurologic exam

- Most accurate of the neurologic exam is the pupillary light reflex
- Lack of corneal reflexes have a relatively low FPR but confidence intervals are high
- Oculocephalic, vestibulo-ocular, cough, gag are not accurate enough to be used as predictors

Neurologic exam

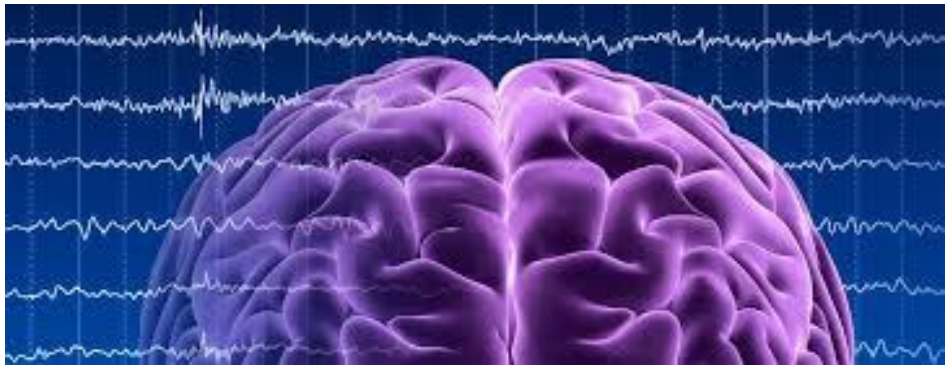
- Motor: absence of motor or extensor posturing is typically associated with a poor outcome however there have been several studies showing unacceptably high FPR and Specificity of only 88%.
- Seems to have increasing low FPR rates as time progresses but in one study showed FPR of 21% at day 3 decreasing to 6% at day 7

Myoclonus

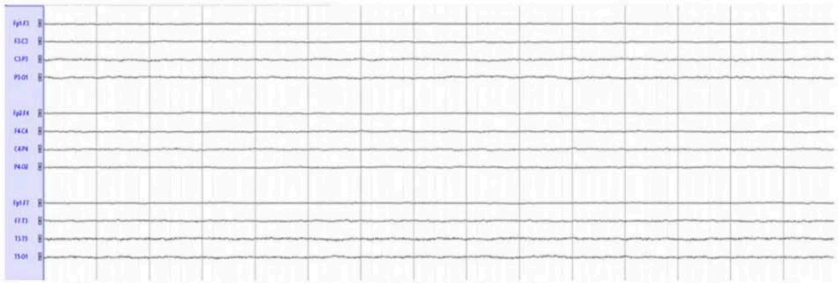
- Present in up to a third of post arrest patients, although typically may be masked by sedation or NMB. It can be focal or diffuse
- Caused by HIBI induced activity of the neurons
- Status myoclonus (SM) is when myoclonus is occurring continuously for >30 minutes
- Can be diagnosed once an EEG has ruled seizures out
- SM although associated with a poor prognosis cannot be used on it's own

EEG

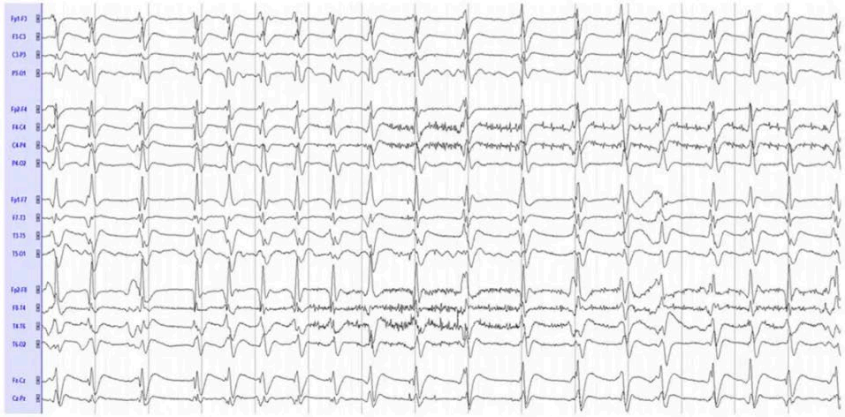
- Should be completed within the 24-72 hrs to rule out non-convulsive status.
- EEG patterns associated with a poor prognosis:
  - Isoelectric patterns, background suppression (>72hrs), burst suppression, Generalized periodic discharges on a suppressed background



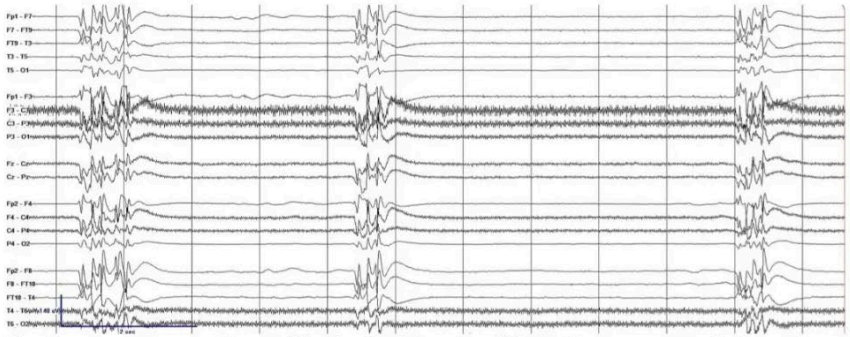
Malignant EEG patterns



Low voltage, no activity (consistent with brain death).



Generalized periodic discharges on a suppressed background. If generalized periodic discharges occur at high frequency, this may resemble status epilepticus.



Burst-suppression pattern with identical bursts. This pattern appears to be unique to

Seizures

- In general clinical status epilepticus is associated with very poor outcomes
- However there can be recovery if status is seen in the absence of other markers of poor outcome*
- Management of the seizures is recommended while other forms of neuroprognostication is ongoing

Electrographic Status Epilepticus

- Depending on the background EEG patient's can have a good recovery with up to 25-40% in some studies.
- There is more clinical equipoise in treatment but in general it is recommended to treat with sedation and anti-epileptics if necessary

Inter-ictal spectrum

Treating Rhythmic and Periodic EEG Patterns in Comatose Survivors of Cardiac Arrest

Authors: Barry J. Ruijter, M.D., Ph.D., Hanneke M. Keijzer, M.Sc., Marleen C. Tjepkema-Cloostermans, Ph.D., Michiel J. Blans, M.D., Albertus Beishuizen, M.D., Ph.D., Selma C. Tromp, M.D., Ph.D., Erik Scholten, M.D., +19 , for the TELSTA Investigators* Author Info & Affiliations

- Rhythmic and periodic patterns are epileptiform patterns that do not meet criteria for seziures. They lie on the ictal-interictal continnum. In this study treatment of these had no improvement in outcome.
- Add study slide in

SSEP

Imaging

How early can we declare brain death?

- We suggest delaying the clinical assessment for at least 48 hr from the time of return of spontaneous circulation post-cardiac arrest for patients with hypoxic-ischemic injury who do not have imaging evidence consistent with devastating brain injury undergoing DNC
- For patients with secondary cardiac arrest associated with other forms of primary devastating brain injury such as traumatic brain injury, massive ischemic stroke, or intracerebral hemorrhage, imaging in these cases almost always confirms the etiology of the clinical picture, especially if there is evidence of cerebral edema, mass effect, and herniation. In these cases, a 24-hr delay before conducting the clinical assessment for DNC may be considered.

BC transplant guidelines

- For Cardiac Arrest: Neurological assessments are unreliable in the acute post-resuscitation phase after cardiac arrest. In cases of acute hypoxic-ischemic brain injury without evidence of devastating brain injury on neuroimaging, clinical evaluation for DNC should be **delayed for 48 hours or an ancillary test could be performed**. Alternatively, if repeat CT scan prior to 48 hours shows devastating injury clinical evaluation can proceed. Examiners are cautioned to review confounding issues in the context of the primary etiology and examination. Clinical judgment is the deciding factor.

a place of mind

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Neurologic Outcomes

- Criteria for likely poor neurologic outcome
  - Absent or extensor motor response to pain and two of
    - Bilateral absent pupillary and corneal reflexes
    - Bilateral absent SSEP N20-response
    - Diffuse anoxic brain injury on CT or MRI
    - Status myoclonus within 48 hours of randomization
    - High levels of NSE
    - EEG with a highly malignant pattern without reactivity to sound or pain

Thank You!

Any questions or comments?