Neuroprognostication following cardiac arrest

Neuro critical care TED

6th May 2021

Aims

- Understand what is meant by hypoxic-ischaemic brain injury (HIBI) after cardiac arrest
- Know the factors that influence neurological outcomes
- Understand the methods used to prognosticate and their caveats
- Be aware of current consensus statements for neuroprognostication following cardiac arrest

Why care about neuroprognostication?

>80% of patients admitted to ICU after OHCA are comatose because of hypoxic–ischaemic brain injury (HIBI)

~2/3rds will die

The majority of deaths result from withdrawal of life-sustaining treatment (WLST) because of a predicted poor neurological outcome

Accurate neuroprognostication is essential

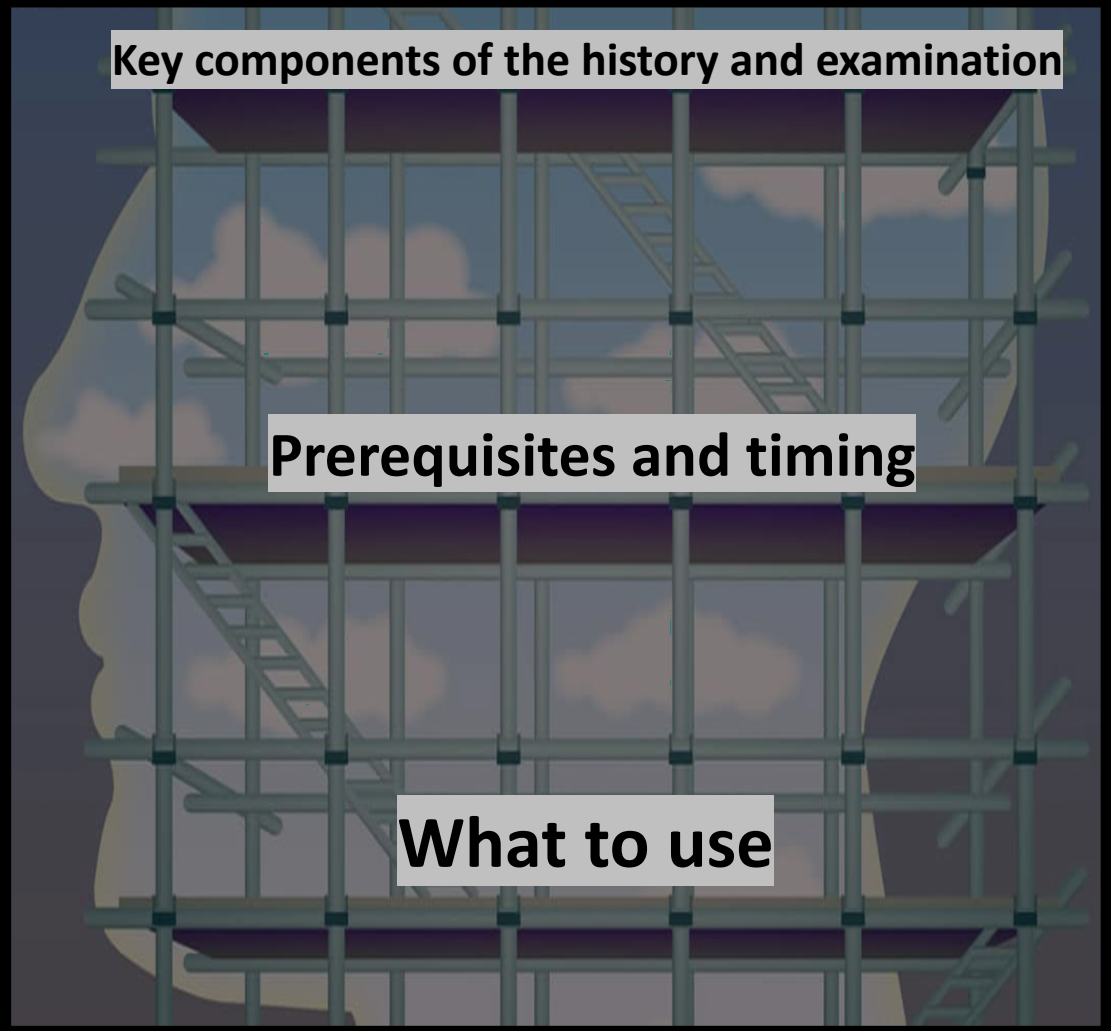
1) To provide correct information for their relatives
2) Avoid both inappropriate WLST or prolonged treatment of patients with no chance of neurologically meaningful survival

Sandroni et al. Prediction of poor neurological outcome in comatose survivors of cardiac arrest: a systematic review *Intensive Care Med (2020) 46:1803–1851*

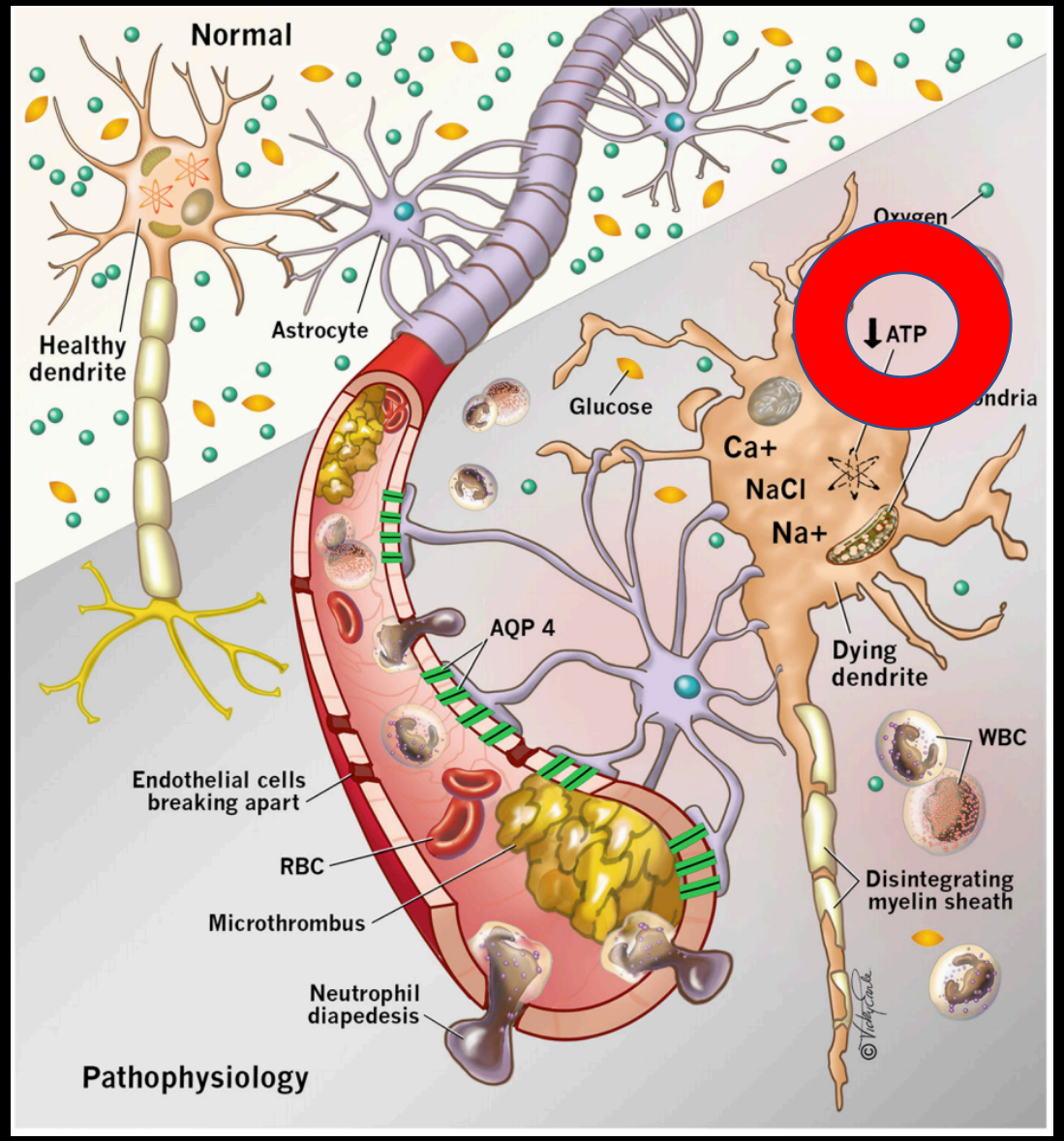
Case example

70F Day 2 following OHCA. Witnessed. Bystander CPR. Initial rhythm VF, shock x 3. ROSC after 15 minutes. PCI LAD. Haemodynamically stable.

How will you approach neuroprognostication on your ward round?



What is hypoxic ischaemic brain injury (HIBI)?

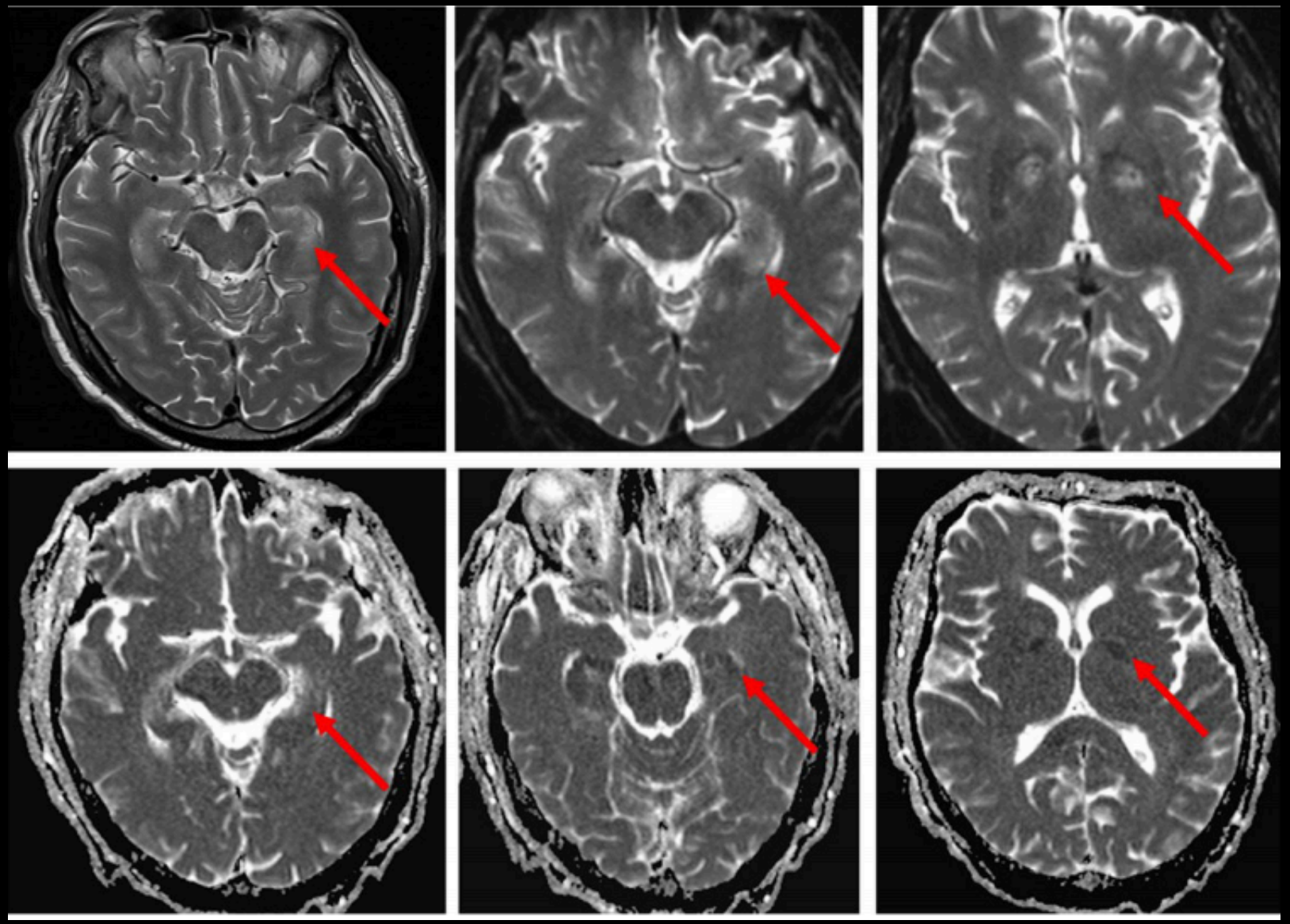


Pathophysiology

Table 2 Pathophysiologic summary of cerebral reperfusion injury after cardiac arrest

Pathophysiology	Mechanisms	Consequences
Endothelial dysfunction	Impaired vasomotor control of blood flow, microthrombi formation, blood-brain barrier disruption	Impaired blood flow in microcirculation and limited oxygen delivery, cerebral edema
Free radical formation	Activation of lytic cellular enzymes	Neuronal apoptosis and cell death
Intracellular Ca^{2+} accumulation,	Mitochondrial toxicity, activation of cellular lytic enzymes	Reduced adenosine triphosphate production, cell death, apoptosis
Impaired nitric oxide,	Vasoconstriction, "no reflow"	Reduced cerebral blood flow, cerebral ischemia
Excitatory neurotransmitter release	Glutamate release	Excitotoxicity, seizures, apoptosis, cell death

Sekhon et al. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model. Critical Care (2017) 21:90 DOI 10.1186/s13054-017-1670-9
Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Böttiger BW, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A Scientific Statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Stroke. Resuscitation. 2008;79:350–79.
Zimmerman JE, Kramer AA, Knaus WA. Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012. Crit Care. 2013;17:R81.



T2-weighted sequences reveal abnormal signalling and diffusion restriction in the **hippocampi and basal ganglia**

The stats

ORIGINAL ARTICLES

Trends in intensive care unit cardiac arrest admissions and mortality in Australia and New Zealand

Lahn D Straney, Janet E Bray, Judith Finn, Stephen Bernard and David Pilcher

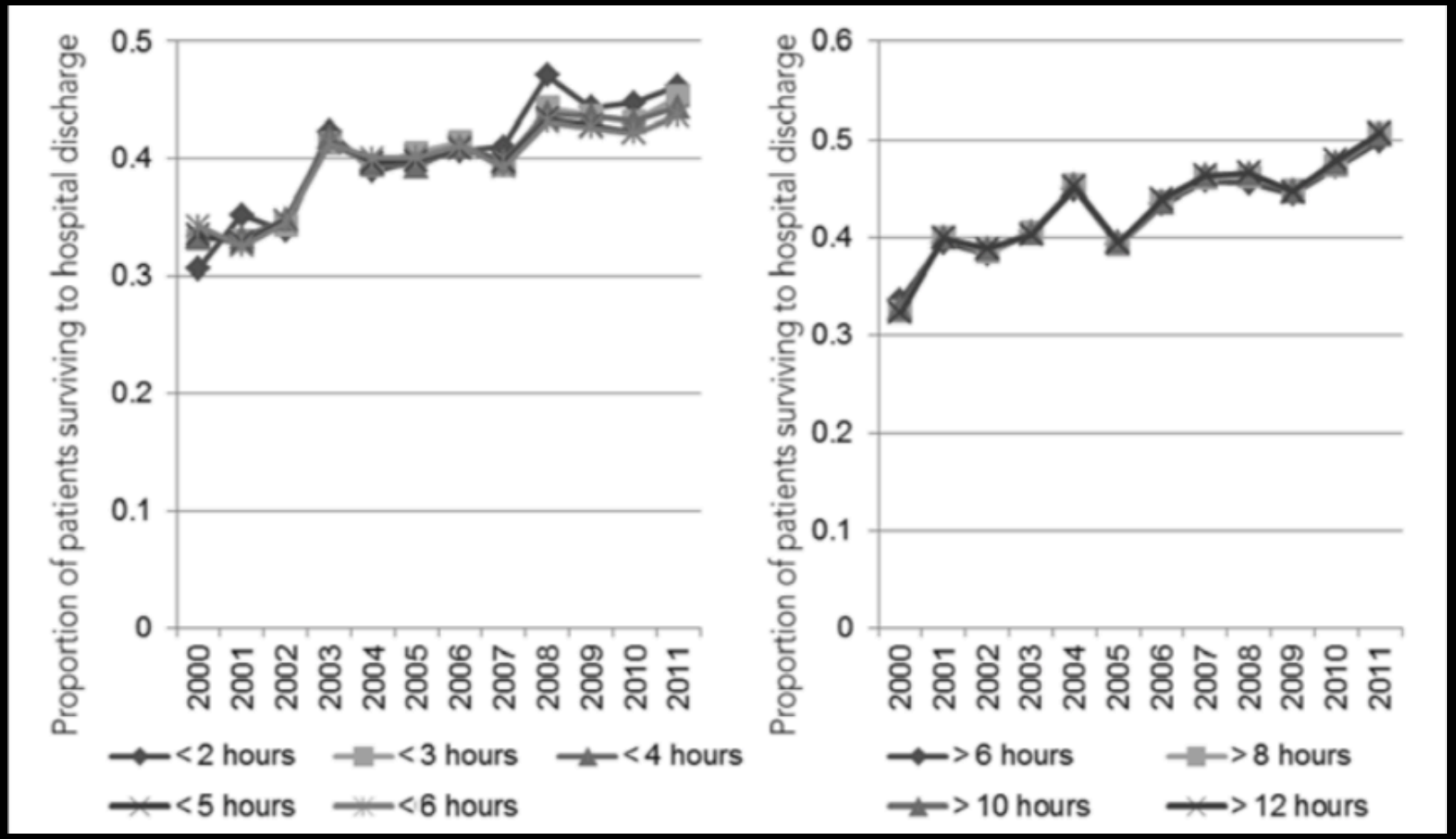
- Overall increase in admissions post cardiac arrest
- ~ 2.5% of all admissions
- Less IHCA and more OHCA admissions over the decade

Table 2. Descriptive statistics for the intensive care units that contributed to data for all years 2000–2011, using method 7 to distinguish OHCA from IHCA

Admissions	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Change 2000–2011	β	95% CI
All															
Volume	38 472	45 806	47 882	50 404	52 437	53 615	55 646	58 660	58 304	62 295	65 781	67 819	29 347	2321	2058 to 2583
Age*	59.7	60.4	60.9	61.2	61.3	61.1	61.3	61.2	61.3	61.1	61.4	61.2	1.6	0.1	0.0 to 0.2
Male (%)	61.1	60.3	60.1	59.6	58.8	58.5	59.2	58.9	58.8	57.9	58.3	57.9	–3.1	–0.3	–0.3 to –0.2
Survival†	83.9	84.6	84.6	85.1	85.6	86.2	86.4	86.6	87.0	87.5	88.2	88.6	4.7	0.4	0.4 to 0.4
CA															
Volume	971	1190	1245	1244	1325	1332	1318	1442	1603	1668	1662	1699	728	61	50 to 71
Vol/1000‡	25.2	26.0	26.0	24.7	25.3	24.8	23.7	24.6	27.5	26.8	25.3	25.1	–0.2	0.0	–0.1 to 0.2
Age*	65.7	65.8	67.8	66.9	65.7	66.4	65.6	65.5	64.2	64.1	64.1	63.5	–2.2	–0.3	–0.4 to –0.1
Male (%)	62.9	61.3	61.4	63.7	62.0	62.2	65.1	65.4	65.8	64.1	65.5	68.1	5.2	0.5	0.3 to 0.7
Survival†	33.0	36.4	36.6	40.1	42.0	39.6	38.6	40.1	42.3	43.0	43.4	44.4	11.4	0.8	0.6 to 1.1
IHCA															
Volume	541	649	747	777	701	704	712	785	846	808	838	822	281	20	12 to 29
Vol/1000‡	14.1	14.2	15.6	15.4	13.4	13.1	12.8	13.4	14.5	13.0	12.7	12.1	–2.0	–0.2	–0.3 to –0.1
Age*	66.0	66.2	68.4	68.1	66.4	67.6	67.1	67.3	65.7	66.2	65.6	64.5	–1.5	–0.2	–0.3 to 0.0
Male (%)	60.3	58.5	57.1	59.7	58.6	59.4	62.4	63.8	65.1	62.7	64.9	67.9	7.6	0.8	0.51 to 1.1
Survival†	31.8	38.6	38.4	39.3	44.4	39.4	40.1	41.6	43.7	44.6	46.3	47.1	15.3	1.0	0.7 to 1.4
OHCA															
Volume	430	541	498	467	624	628	606	657	757	860	824	877	447	40	32 to 49
Vol/1000‡	11.2	11.8	10.4	9.3	11.9	11.7	10.9	11.2	13.0	13.8	12.5	12.9	1.8	0.2	0.1 to 0.4
Age*	64.7	65.1	66.5	64.4	64.9	65.4	63.3	62.8	62.1	61.5	62.0	62.0	–2.7	–0.4	–0.5 to –0.3
Male (%)	66.8	63.1	66.6	69.2	65.1	65.5	69.9	66.6	67.1	65.4	65.8	70.6	3.8	0.2	–0.2 to 0.5
Survival†	32.8	35.0	34.1	39.8	38.2	40.6	38.2	38.7	42.7	43.6	42.2	44.2	11.4	0.9	0.7 to 1.2

β = mean annual change. CA = cardiac arrest. IHCA = in-hospital CA. OHCA = out-of-hospital CA. * Mean (years). † Survival to hospital discharge (%). ‡ Volume/1000 admissions.

Crit Care Resusc 2014; 16: 104–111



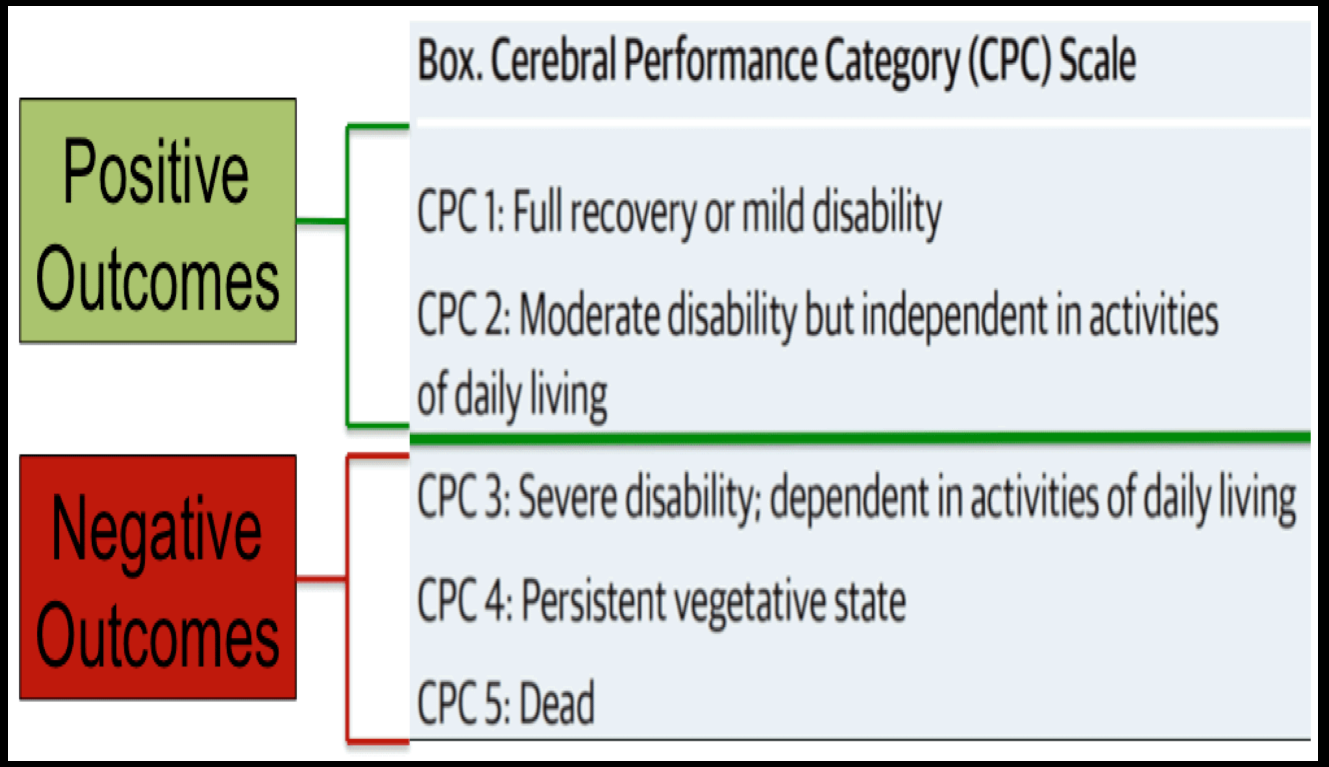
Increasing survival to hospital discharge

OHCA 33.2% in 2000 to 45.3% in 2011

IHCA : 32.7% in 2000 to 50.6% in 2011

What about survival with good neurological outcome?

How is it measured?



modified Rankin Score (mRS)

Score	Description
0	No symptoms at all
1	No significant disability despite having symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance, and unable to attend own bodily needs without assistance
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention
6	Dead

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D., David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sci., Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D., Jesper Kjaergaard, M.D., D.M.Sci., Michael Kuiper, M.D., Ph.D., Tommaso Pellis, M.D., Pascal Stammet, M.D., Michael Wanscher, M.D., Ph.D., Matt P. Wise, M.D., D.Phil., Anders Åneman, M.D., Ph.D., Nawaf Al-Subaie, M.D., Søren Boesgaard, M.D., D.M.Sci., John Bro-Jeppesen, M.D., Iole Brunetti, M.D., Jan Frederik Bugge, M.D., Ph.D., Christopher D. Hingston, M.D., Nicole P. Juffermans, M.D., Ph.D., Matty Koopmans, R.N., M.Sc., Lars Køber, M.D., D.M.Sci., Jørund Langørgen, M.D., Gisela Lilja, O.T., Jacob Eifer Møller, M.D., D.M.Sci., Malin Rundgren, M.D., Ph.D., Christian Rylander, M.D., Ph.D., Ondrej Smid, M.D., Christophe Werer, M.D., Per Winkel, M.D., D.M.Sci., and Hans Friberg, M.D., Ph.D., for the TTM Trial Investigators*

- Overall survival ~50%
- ~ 50% of survivors had a “good neurological outcome”
- This was a trial predominantly of shockable OHCA (80% had shockable rhythms)

Table 3. Neurologic Scores.*

Variable	33°C Group	36°C Group
CPC at follow-up†		
Total no. of patients	469	464
Category — no. (%)		
1	195 (42)	183 (39)
2	23 (5)	39 (8)
3	17 (4)	20 (4)
4	6 (1)	2 (0.5)
5	228 (49)	220 (47)
P value for trend	0.85	
Modified Rankin scale score at follow-up†		
Total no. of patients	469	464
Score — no. (%)		
0	88 (19)	89 (19)
1	69 (15)	83 (18)
2	50 (11)	34 (7)
3	17 (4)	19 (4)
4	8 (2)	11 (2)
5	9 (2)	8 (2)
6	228 (49)	220 (47)
P value for trend	0.67	

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm

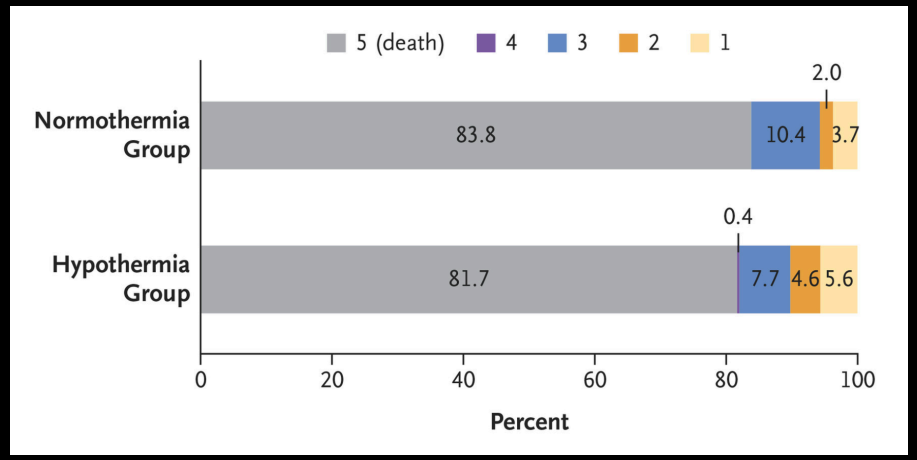
J.-B. Lascarrou, H. Merdji, A. Le Gouge, G. Colin, G. Grillet, P. Girardie, E. Coupez, P.-F. Dequin, A. Cariou, T. Boulain, N. Brule, J.-P. Frat, P. Asfar, N. Pichon, M. Landais, G. Plantefeve, J.-P. Quenot, J.-C. Chakarian, M. Sirodot, S. Legriel, J. Letheulle, D. Thevenin, A. Desachy, A. Delahaye,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

Overall < 20% survival in non-shockable rhythms

Of those that survive very small proportion have good neurological outcome

Table 2. Neurologic Outcomes and Hospitalization Characteristics.*

Outcome	Hypothermia (N=284)	Normothermia (N=297)	Difference or Hazard Ratio (95% CI)
CPC score of 1 or 2 on day 90 — no. (%)	29 (10.2)	17 (5.7)	4.5 (0.1 to 8.9)†
CPC score distribution on day 90 — no. (%)			
CPC score of 1	16 (5.6)	11 (3.7)	
CPC score of 2	13 (4.6)	6 (2.0)	
CPC score of 3	22 (7.7)	31 (10.4)	
CPC score of 4	1 (0.4)	0	
CPC score of 5	231 (81.3)	247 (83.2)	
Loss to follow-up	1 (0.4)	2 (0.7)	
Death by day 90 — no. (%)	231 (81.3)	247 (83.2)	−1.9 (−8.0 to 4.4)†
Death in the ICU — no. (%)	222 (78.2)	236 (79.5)	0.93 (0.78 to 1.10)‡
Duration of mechanical ventilation — days			
Median	4.5	4.0	
Interquartile range	2.0 to 7.0	2.0 to 7.0	
Length of stay in ICU — days			
Median	4.0	4.0	
Interquartile range	2.0 to 7.0	2.0 to 6.0	
Survival to ICU discharge — no. (%)	62 (21.8)	61 (20.5)	1.07 (0.75 to 1.52)‡
Duration of mechanical ventilation — days			
Median	11.0	10.0	
Interquartile range	6.0 to 24.0	4.0 to 27.0	
Length of stay in ICU — days			
Median	6.0	6.0	
Interquartile range	4.0 to 18.0	2.0 to 21.0	
Survival to hospital discharge — no. (%)	56 (19.7)	50 (16.8)	1.19 (0.81 to 1.74)‡



What factors determine neurological outcome?

PREARREST AND INTRAARREST FACTORS

Bottom Line : No single factor from the history is reliable enough for neuroprognostication

This is why inclusion and exclusion criteria for E-CPR varies so widely

Standards for Studies of Neurological Prognostication in Comatose Survivors of Cardiac Arrest
A Scientific Statement From the American Heart Association Circulation. 2019;140:e517–e542

That's not the same as saying certain factors are not important

- **Rhythm** – non- shockable rhythms have worse outcomes
  - Rule of thumb in OHCA – VF/VT ~ 40%, PEA ~ 10%, Asystole ~1%
- **Duration of arrest – THE LOW FLOW TIME** - > 35 minutes drop off in survival and neurological outcomes
- **Unwitnessed + No Bystander CPR – THE NO FLOW TIME** both are associated with worse outcomes
- **Significant patient comorbidity + Age**
  - > 80yrs – steep increase in mortality
  - Age doesn't seem to predict neurological outcome

Rogove HJ, Safar P, Sutton-Tyrrell K, Abramson NS. Old age does not negate good cerebral outcome after cardiopulmonary resuscitation: analyses from the brain resuscitation clinical trials. The Brain Resuscitation Clinical Trial I and II Study Groups. Crit Care Med. 1995 Jan;23(1):18-25.

Bunch, T. Jared, et al. "Outcomes and in-hospital treatment of out-of-hospital cardiac arrest patients resuscitated from ventricular fibrillation by early defibrillation." *Mayo Clinic Proceedings*. Vol. 79. No. 5. Elsevier, 2004.

Engdahl, Johan, et al. "Can we define patients with no and those with some chance of survival when found in asystole out of hospital?." *The American journal of cardiology* 86.6 (2000): 610-614.

Duration of resuscitation efforts and survival after in-hospital cardiac arrest: an observational study

*Zachary D Goldberger, Paul S Chan, Robert A Berg, Steven L Kronick, Colin R Cooke, Mingrui Lu, Mousumi Banerjee, Rodney A Hayward, Harlan M Krumholz, Brahmajee K Nallamothu, for the American Heart Association Get With The Guidelines—Resuscitation (formerly the National Registry of Cardiopulmonary Resuscitation) Investigators**

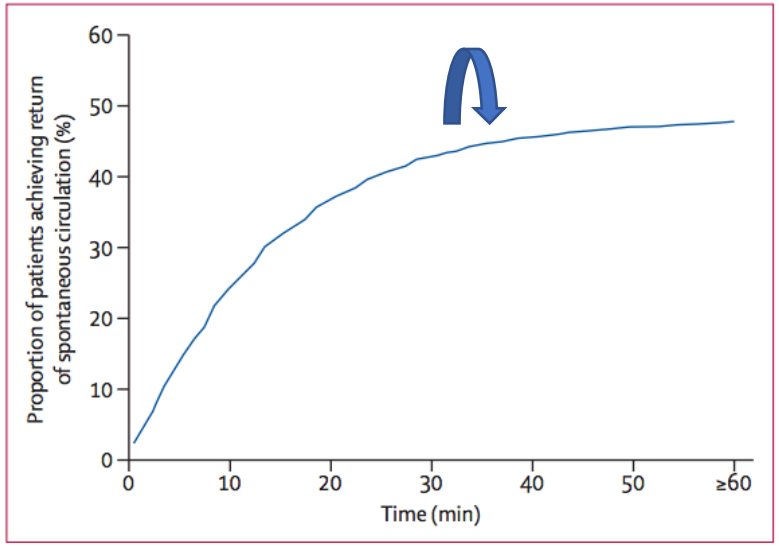


Figure 1: **Cumulative proportion of patients achieving return of spontaneous circulation**

31 198 of 64 339 (48·5%) patients achieved return of spontaneous circulation, 9912 (15·4%) survived to discharge

20.1% Non shockable, 79.9% Shockable

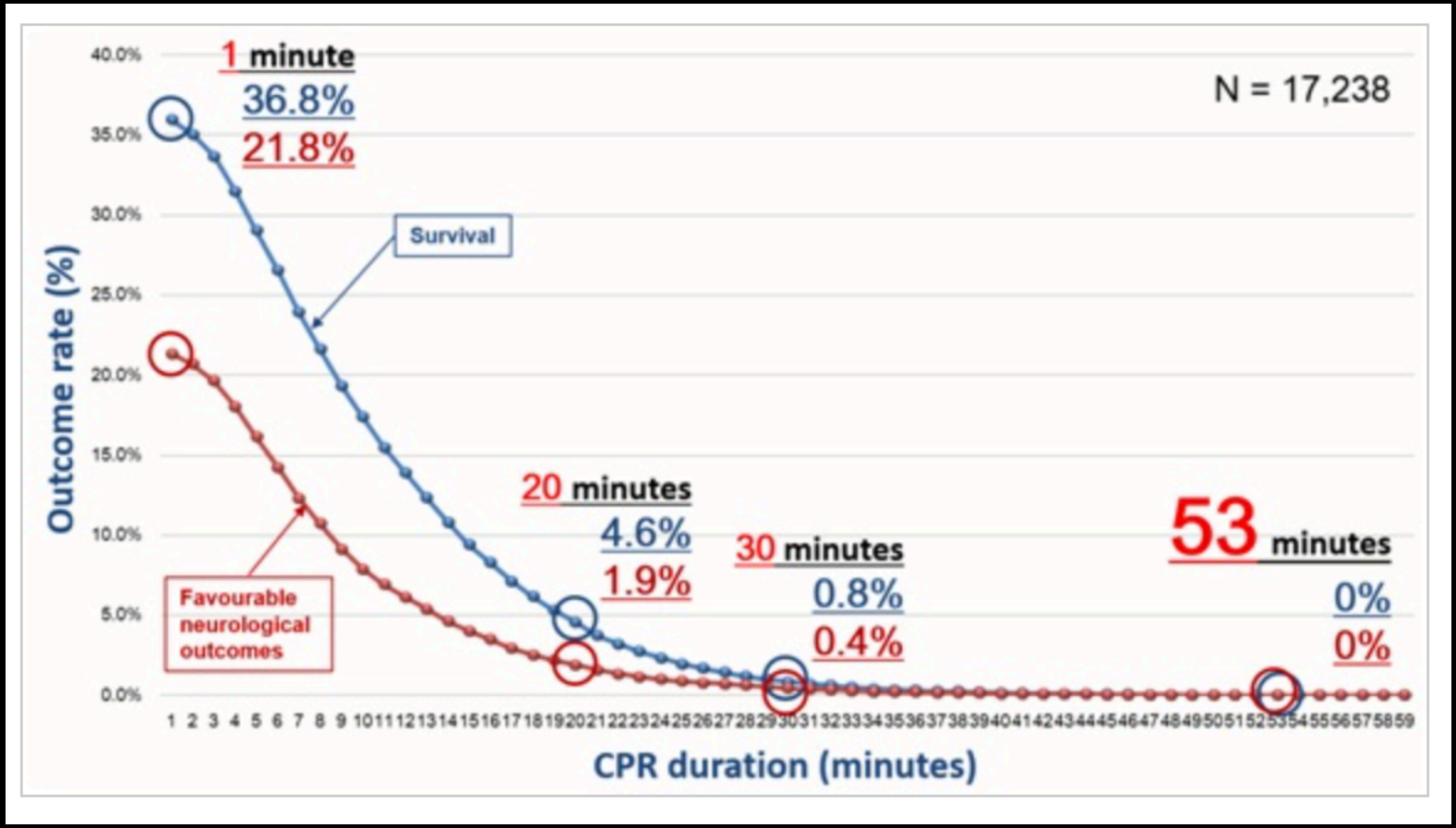
TAKE HOME – IN MOST CASES IF YOU HAVENT GOT ROSC WITHIN 35 MINS FOR AN IN-HOSPITAL CA YOU'RE UNLIKELY TO ACHIEVE IT…

Lancet 2012; 380: 1473–81

Relationship Between the Duration of Cardiopulmonary Resuscitation and Favorable Neurological Outcomes After Out-of-Hospital Cardiac Arrest: A Prospective, Nationwide, Population-Based Cohort Study

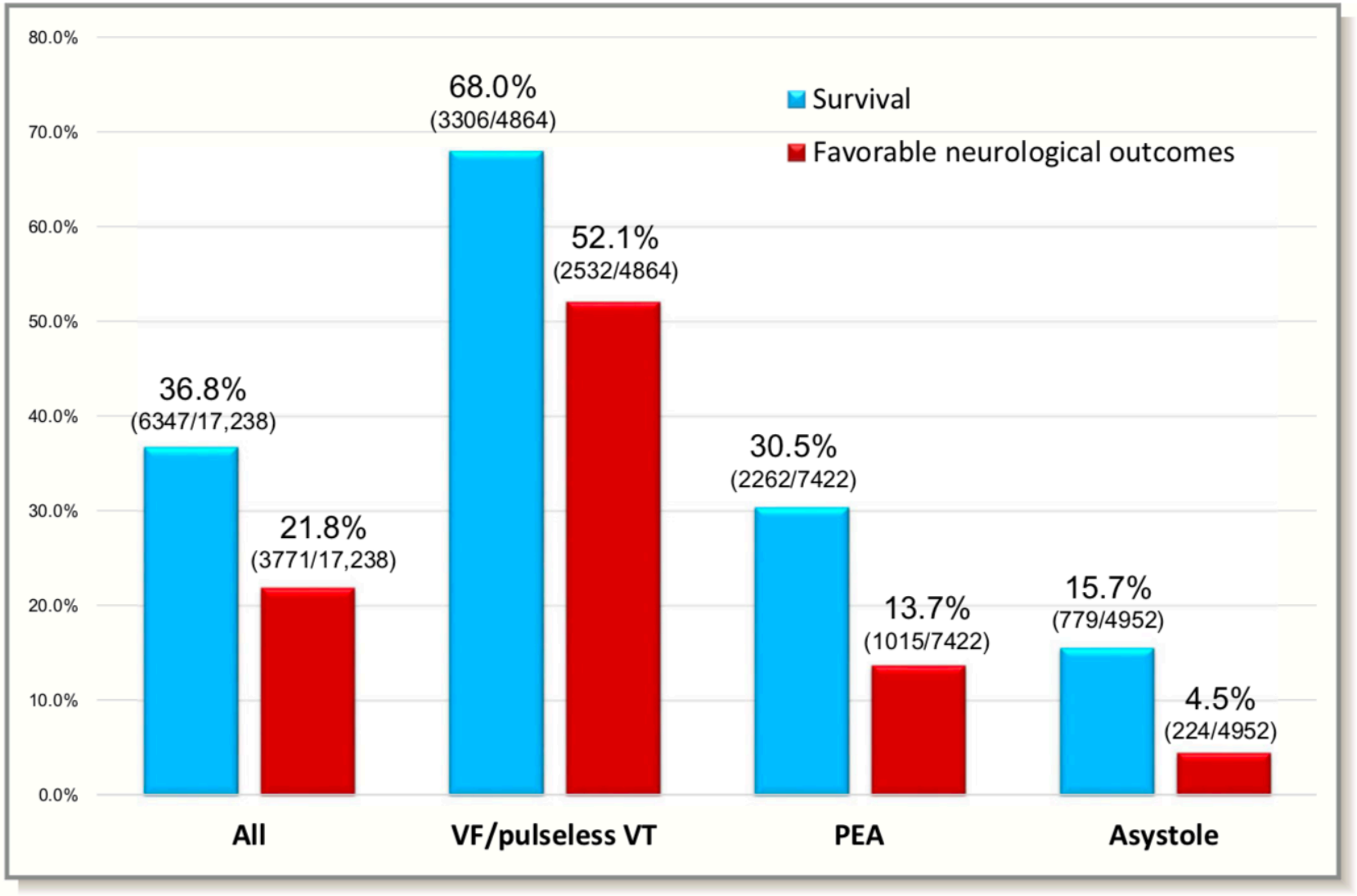
Yoshikazu Goto, MD, PhD; Akira Funada, MD, PhD; Yumiko Goto, MD, PhD

- No patient with a CPR duration of ≥53 minutes survived one month after cardiac arrest



J Am Heart Assoc. 2016;5:e002819

CPR Duration for Cardiac Arrest *Goto et al*



E-CPR

CHEER 3 Trial
Inclusion
Age 18 to 65 years
Witnessed cardiac arrest (bystander or paramedic)
Time from arrest to commence chest compressions of less than 5 minutes
Duration of cardiac arrest between 20 and 45 minutes
Initial cardiac rhythm of Ventricular Fibrillation/pulseless Ventricular Tachycardia/Pulseless Electrical Activity
In cardiac arrest on arrival of ECMO team

Exclusion
Traumatic arrest including hanging
Known to have significant life-limiting co-morbidities (eg COPD/cirrhosis/dementia) or terminal illness

POSTARREST EVALUATION IN ICU: NEUROLOGICAL ASSESSMENT IN COMATOSE SURVIVORS

Intensive Care Med (2021) 47:369–421
https://doi.org/10.1007/s00134-021-06368-4

CONFERENCE REPORTS AND EXPERT PANEL

European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation care

Jerry P. Nolan[1,2*], Claudio Sandroni[3,4], Bernd W. Böttiger[5], Alain Cariou[6], Tobias Cronberg[7], Hans Friberg[8], Cornelia Genbrugge[9,10], Kirstie Haywood[11], Gisela Lilja[12], Véronique R. M. Moulaert[13], Nikolaos Nikolaou[14], Theresa Mariero Olasveengen[15], Markus B. Skrifvars[16], Fabio Taccone[17] and Jasmeet Soar[18]

Nolan et al. Intensive Care Med (2021) 47:369–421

AND SO IS PRECISION

High specificity and precision essential

Lowest possible false positive rate (FPR) with narrow CIs

72 hours *

Why is 72 hours the magic number?

- Following global post-anoxic injury, the brain will make a gradual recovery. Brainstem reflexes return first, then the motor response to pain and, finally, cortical activity and consciousness
- This process is completed within 72h from arrest

- We also need residual sedation and paralysis to have worn off

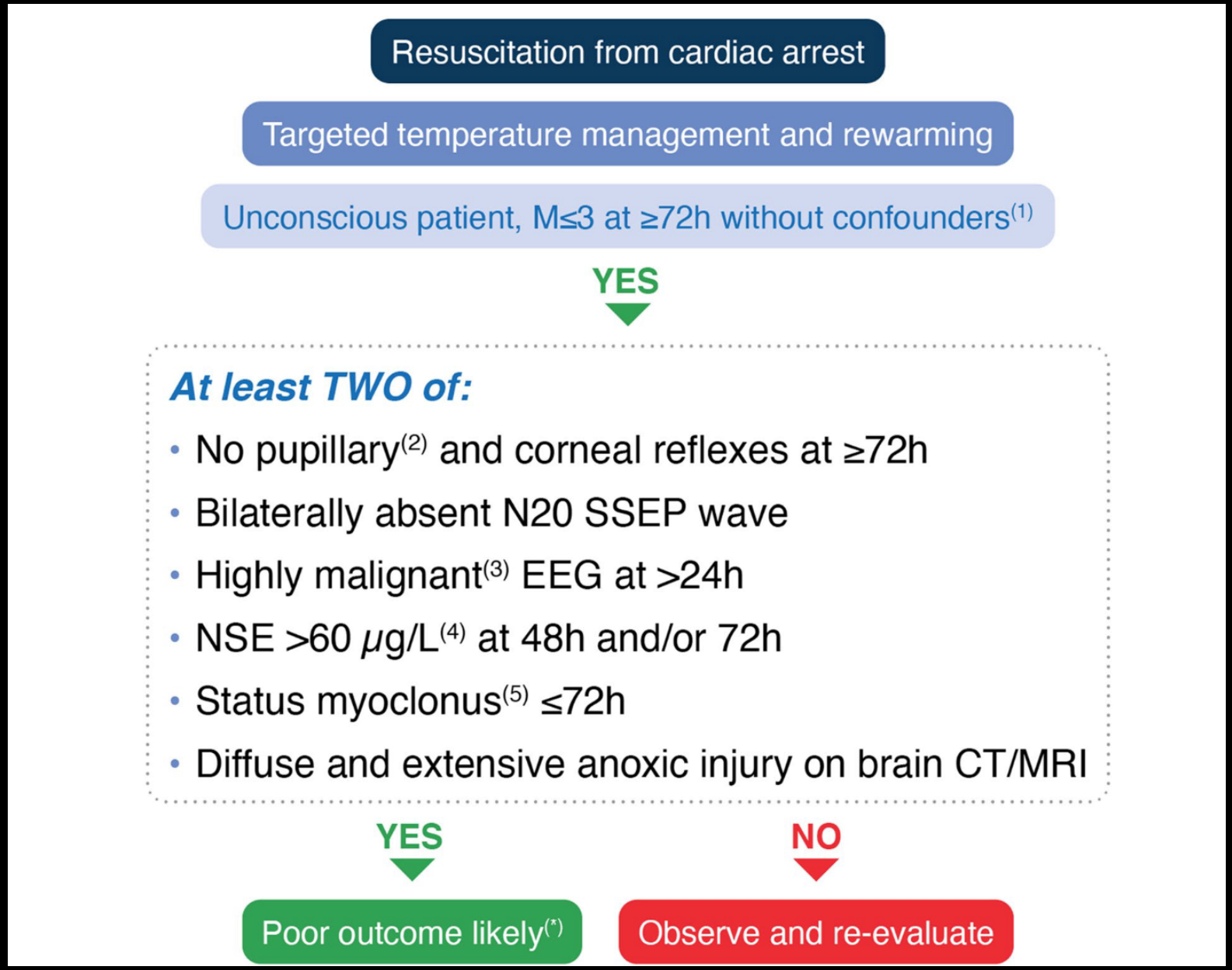
What about in those who have had TTM?

- The '72 hour clock' starts after they are normothermic (doesn't matter so much then if TTM was at 36)

*** You must have a good reason to neuroprognosticate before this time**

*** Not really a magic number, often we need longer**

Jorgensen EO, Holm S. The natural course of neurological recovery following cardiopulmonary resuscitation. Resuscitation 1998;36:111–22.



Major confounders may include sedation, neuromuscular blockade, hypothermia, severe hypotension, hypoglycaemia, sepsis, and metabolic and respiratory derangements

The clinical tests

1) Pupillary and corneal reflexes

Pupils

- A bilaterally absent PLR has low specificity for predicting poor outcome in the first hours after ROSC, accuracy progressively increases with time
- Absent PLR = 100% specificity with 20–25% sensitivity after 96 hours from ROSC
- Use of automated pupillometer is recommended

Corneal

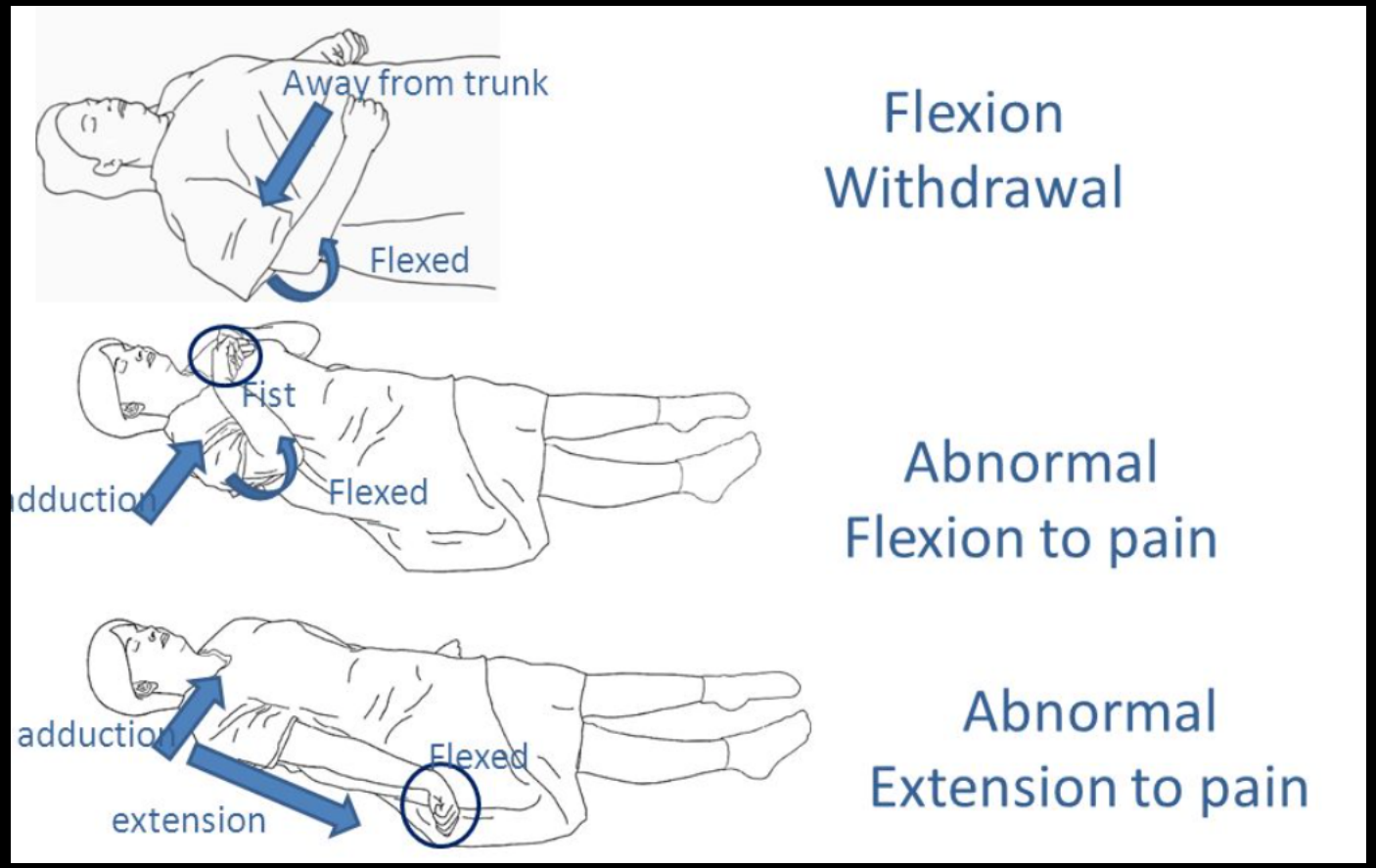
- Absent CR predicts poor neurological outcome after 72 h from ROSC with 100% specificity and 25–40% sensitivity

TAKE HOME

- **DON'T USE EITHER AS A MARKER OF POOR NEUROLOGICAL OUTCOME IN FIRST FEW HOURS. WAIT 72 HOURS**

Nolan et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation careIntensive Care Med (2021) 47:369–421

2) The motor score



A poor motor response has a relatively low specificity, but a high sensitivity for prediction of poor neurological outcome after cardiac arrest.

Therefore, it can be used to identify patients needing prognostication.

TAKE HOME

- **HIGH FALSE POSITIVE RATE**
- **DON'T USE MOTOR SCORE IN ISOLATION**

Nolan et al. European Resuscitation Council and European Society of Intensive Care Medicine guidelines 2021: post-resuscitation careIntensive Care Med (2021) 47:369–421

3) What about myoclonus?

Sudden, brief, involuntary jerks caused by muscular contractions or inhibitions

Presence of myoclonus within 96 h from ROSC in patients who are comatose is associated with poor neurological outcome in most cases

However, a false positive rate of up to 22% has been described

Therefore, CAUTION is needed

Table 12 Accuracy of clinical examination. Myoclonus

Author, year	Definition	Sample size, *n*	Timing	Timing outcome	TP	FP	FN	TN	Sensitivity % [95% CI]	FPR % [95% CI]
≤ 24 h										
Sadaka, 2015 [109]	(1)	58	≤ 24 h	HD	9	1	24	24	27.3 [13.3–45.5]	4 [0.1–20.4]
≤ 48 h										
Fatuzzo, 2018 [96]	N/A	493	≤ 48 h	3 mo	82	6	184	221	30.8 [25.3–36.8]	2.6 [1–5.7]
≤ 72 h										
Kongpolprom, 2018 [26]	N/A	51	48-72 h	HD	15	2	27	7	35.7 [21.6–52]	22.2 [2.8–60]
Sivaraju, 2015 [111]	N/A	100	≤ 72 h	HD	23	4	48	25	32.4 [21.8–44.5]	13.8 [3.9–31.7]
Maia, 2013 [104] (2)	N/A	26	≤ 72 h	6 mo	8	0	10	8	44.4 [21.5–69.2]	0 [0–31.2]
≤ 96 h										
Reynolds, 2018 [32]	N/A	583	≤ 96 h	HD	87	3	390	103	18.2 [14.9–22]	2.8 [0.6–8]

Sandroni et al. Intensive Care Med (2020) 46:1803–1851

Kongpolprom N, Cholkraisuwat J (2018) Neurological prognostications for the therapeutic hypothermia among comatose survivors of cardiac arrest. Indian J Crit Care Med 22:509–518

Status Myoclonus is different

Continuous and generalized myoclonus persisting for 30 min or more

Low FP rate, 99-100% specificity for poor outcome

Table 13 Accuracy of clinical examination. Status myoclonus

Author, year	Definition	Sample size, *n*	Timing	Timing outcome	TP	FP	FN	TN	Sensitivity % [95% CI]	FPR % [95% CI]
≤ 24 h										
Ruknuddeen, 2015 [35]	(1)	121	≤ 24 h	HD	52	0	54	15	49.1 [39.2–59]	0 [0–18.1]
Lybeck, 2017 [27]	(2)	933	≤ 24 h	6 mo	28	1	465	439	5.7 [3.8–8.1]	0.2 [0–1.3]
≤ Day 7										
Lybeck, 2017 [27]	(2)	933	≤ Day 7	6 mo	60	1	433	439	12.2 [9.4–15.4]	0.2 [0–1.3]

Recommended - EEG in patients with post-arrest myoclonus

1) Identify an associated epileptiform activity
2) Detect signs associated with potential recovery

Sandroni et al. Intensive Care Med (2020) 46:1803–1851

Lance-Adams syndrome

is rare but don’t forget about it

Less frequent form of myoclonus usually **developing in a patient who has regained consciousness**

It is more common after hypoxic cardiac arrest

Mainly affects the limbs where it is induced by purposeful actions or sensory stimulation.

It may be disabling and often becomes chronic

Aicua Rapun I, Novy J, Solari D, Oddo M, Rossetti AO (2017) Early Lance– Adams syndrome after cardiac arrest: prevalence, time to return to awareness, and outcome in a large cohort. Resuscitation 115:169–172

A brief word on seizures post cardiac arrest

Seizures are reported in 20–30% of cardiac arrest patients in the ICU and are usually a sign of a severe HIBI

Variety of types – myoclonus, focal, GTC, mixture – EEG or clinical diagnosis

Often unmasked during sedation holds

Shivering is a seizure mimic

How should we manage them?

No role for seizure prophylaxis

Treat seizures with Keppra or sodium valporate, not phenytoin (more hypotension)

EEGs are important tool- no evidence to support cEEG

An assessment of the prognosis and potential for an eventual good outcome are central components of the treatment strategy

The ancillary tests

THE EEG (for intensivists)

Absence of EEG background reactivity or burst-suppression on EEG at ≥ 24 h from ROSC
“Highly malignant”

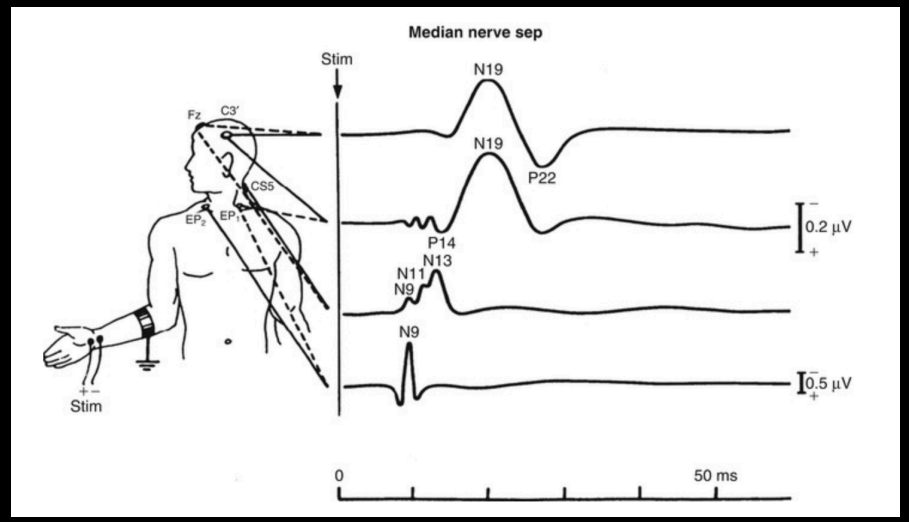
Electrographic status epilepticus is generally but not always bad

Ideally performed off sedation
Don’t use in isolation

The main aspects when assessing EEG are the background activity, superimposed discharges and reactivity

Somatosensory evoked potentials

Bilaterally absent N20 wave of somatosensory evoked potential (SSEP) at≥24 h from ROSC predict poor outcome



Biomarkers

Neuron Specific Enolase

Within 72 h after ROSC a high NSE in combination with other tests predicts poor outcome

There is no consensus on a threshold value

? > 60ug/L

SSEP

Most extensively studied…

Table 17 Evoked potentials. Bilaterally absent N20 SSEP wave

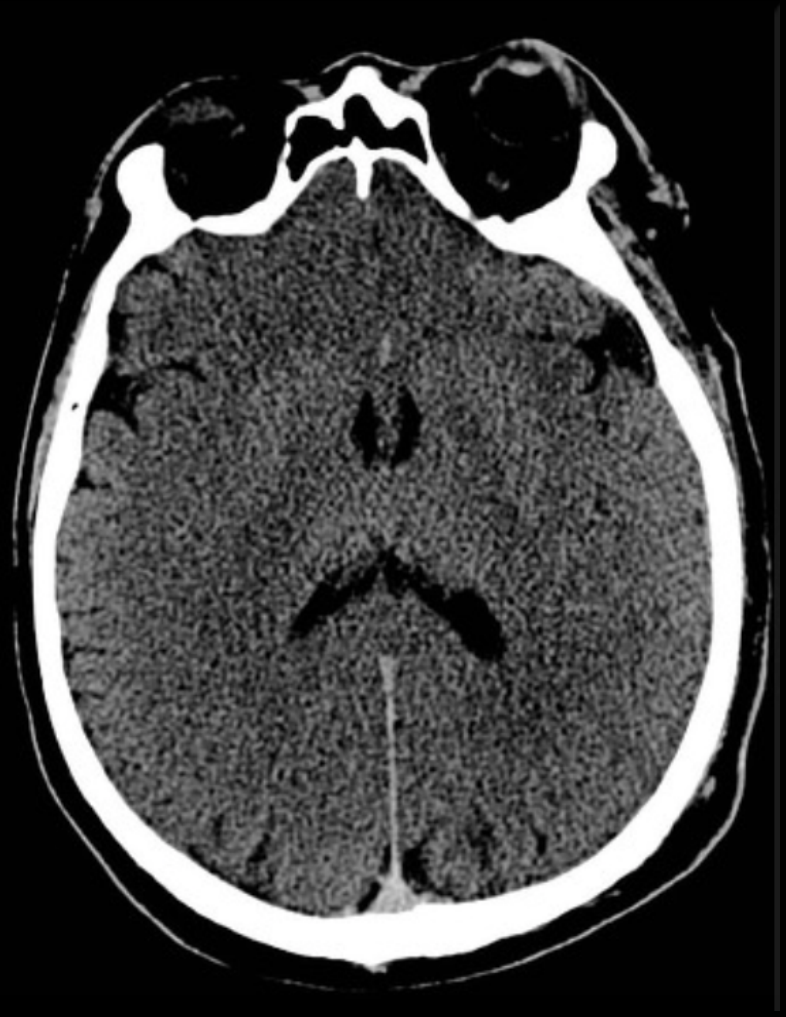
Author, year	Sample size, *n*	Timing	Timing outcome	TP	FP	FN	TN	Sensitivity % [95% CI]	FPR % [95% CI]
< 24 h									
Grippo, 2017 [59]	46	6-12 h	6 mo	16	0	17	13	48.5 [30.8–66.5]	0 [0–20.6]
Scarpino, 2020 [69]	218	12 h	6 mo	68	0	64	86	51.5 [42.7–60.3]	0 [0–3.4]
Grippo, 2017 [59]	78	18-24 h	6 mo	31	0	23	24	57.4 [43.2–70.8]	0 [0–11.7]
Choi, 2017 [91]	80	< 24 h	HD	30	0	22	28	57.7 [43.2–71.3]	0 [0–10.1]
Maciel, 2017 [64]	41	< 24 h	HD	12	0	24	5	33.3 [18.6–51]	0 [0–45.1]
Scarpino, 2019 [110]	346	< 24 h	6 mo	112	0	146	88	43.4 [37.3–49.7]	0 [0–3.3]
24–48 h									
Fatuzzo, 2018 [96]	457	36-48 h	3 mo	115	1	129	212	47.1 [40.7–53.6]	0.5 [0–2.6]
Leao, 2015 [62]	67	24-48 h	6 mo	10	6	45	6	18.2 [9.1–30.9]	50 [21.1–78.9]
0–72 h									
Maia, 2013 [104] ([1])	17	0–72 h	6 mo	7	0	5	5	58.3 [27.7–84.8]	0 [0–45.1]
Dhakal, 2016 [94]	35	24-72 h	HD	15	2	12	6	55.6 [35.3–74.5]	25 [3.2–65.1]
48–72 h									
De Santis, 2017 [93]	65	48-72 h	3 mo	7	0	11	47	38.9 [17.3–64.3]	0 [0–6.2]
Grippo, 2017 [59]	76	48-72 h	6 mo	25	0	36	15	41 [28.6–54.3]	0 [0–18.1]
Kim, 2018 [101]	127	48-72 h	1 mo	50	0	25	52	66.7 [54.8–77.1]	0 [0–5.6]
Oddo, 2018 [106]	188	48-72 h	3 mo	64	0	69	55	48.1 [39.4–56.9]	0 [0–5.3]
Ruijter, 2019 [68]	850	48-72 h	6 mo	123	0	332	395	27 [23–31.4]	0 [0–0.8]
48–96 h									
Choi, 2017 [91]	81	48-96 h	HD	32	0	22	27	59.3 [45–72.4]	0 [0–10.5]
72 h									
Hirsch, 2020 [97]	24	72 h	6 mo	12	0	11	1	52.2 [30.6–73.2]	0 [0–95]
Scarpino, 2020 [69]	240	72 h	6 mo	87	0	79	74	52.4 [44.5–60.2]	0 [0–4]
> 72 h									
Dragancea, 2015 [95]	201	> 72 h	6 mo	74	1	88	38	45.7 [37.8–53.7]	2.6 [0.1–13.5]
Huntgeburth, 2014 [99] ([1])	40	> 72 h	2 mo	9	0	21	10	30 [14.7–49.4]	0 [0–25.9]
Day 4–6									
Kim, 2018 [60]	116	Day 4	HD	56	0	25	35	69.1 [57.9–78.9]	0 [0–8.2]
Nakstad, 2020 [105]	40	Day 5 (3.6–6.5)	6 mo	8	0	15	17	34.8 [16.4–57.3]	0 [0–16.2]

Imaging

Hypoxic–ischaemic brain injury causes cytotoxic and vasogenic oedema

CT - loss of Grey white matter differentiation and swelling with effacement of cortical sulci

MRI - hyperintensity on diffusion- weighted imaging (DWI) sequences



Associated with poor outcomes

CT showing presence of a marked reduction of the grey matter/white matter (GM/WM) ratio on brain CT **within 72 h after ROSC**

MRI showing extensive diffusion restriction on brain MRI at **2–7 days after ROSC**

Their major limitation is the lack of standardisation of measurement techniques

Imaging

TTM trial cohort showed that generalised oedema on brain CT detected visually by local radiologists without formal GWR measurement predicted poor neurological outcome with ~ 97-100% specificity

But at 24 hours sensitivity is very low ~14%, increases to around 50% after 24 hours

Take home

If there is significant swelling it generally means a poor outcome, if it is normal it doesn't exclude poor neurological outcome

Nolan et al. Intensive Care Med (2021) 47:369–421

How many progress to brain death?

Brain death occurs in **5–10%** of patients who die after cardiac arrest resuscitated with conventional CPR

(25% in ECPR cohort)

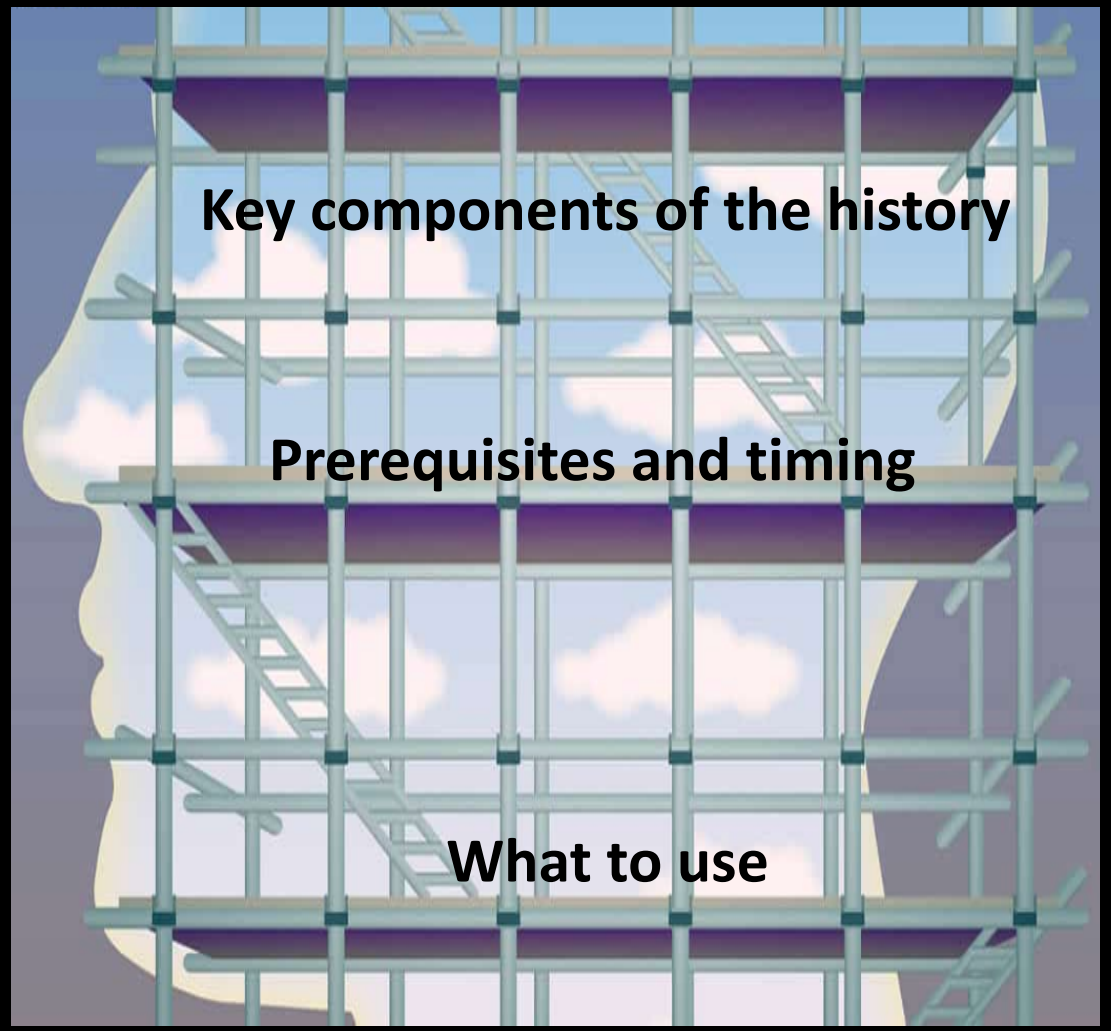
In most cases, brain death occurs during the first 3–4 days after ROSC

Sandroni C, D'Arrigo S, Callaway CW et al (2016) The rate of brain death and organ donation in patients resuscitated from cardiac arrest: a systematic review and meta-analysis. Intensive Care Med 42:1661–1671

Case example

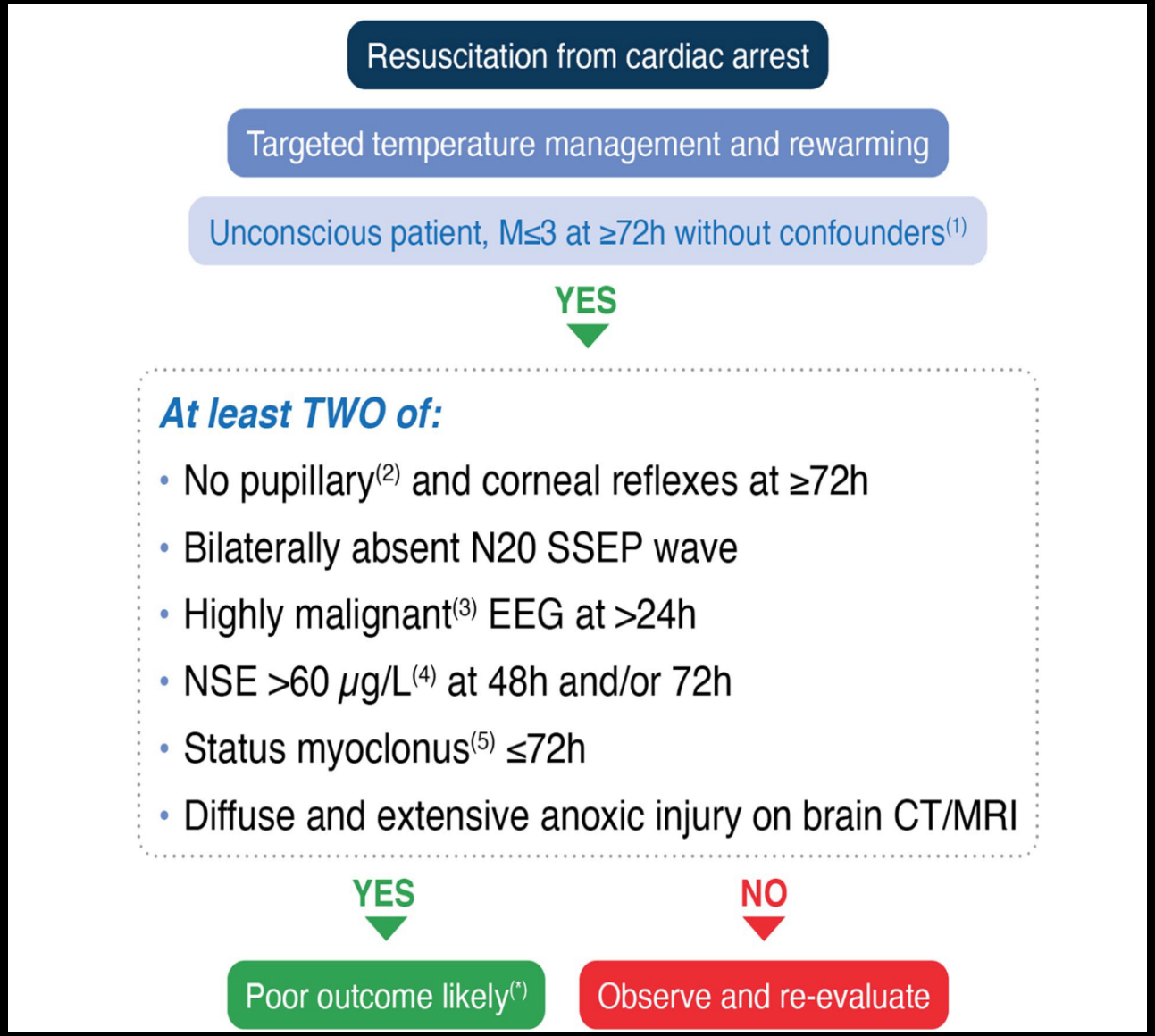
70F Day 2 following OHCA. Witnessed. Bystander CPR. Initial rhythm VF, shock x 3. ROSC after 15 minutes. PCI LAD. Haemodynamically stable.

How will you approach neuroprognostication on your ward round?



Key things

- Too early
- Ensure there are no confounders
- Ensure accuracy of the history
- Clarify pre-morbid status and wishes
- Family, are expectations commensurate with medical team
- **Then use your tool kit….**



In summary

Know what is useful for neuroprognostication

Never rely on a single parameter, always multimodal

Be aware of self- fulfilling prophecy but also be mindful of futile care