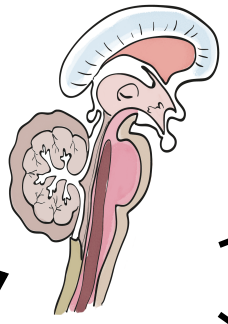
Clinical Examination
&
Pupillometry

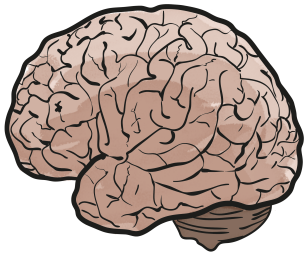
Tobias Cronberg
Associate professor
Department of Neurology
Skåne University Hospital
Department of Clinical Sciences
Lund University, Sweden

Natural course of neurological recovery after resuscitation

Brain stem

Cortex





Consciousness

Cardiac Arrest → COMA

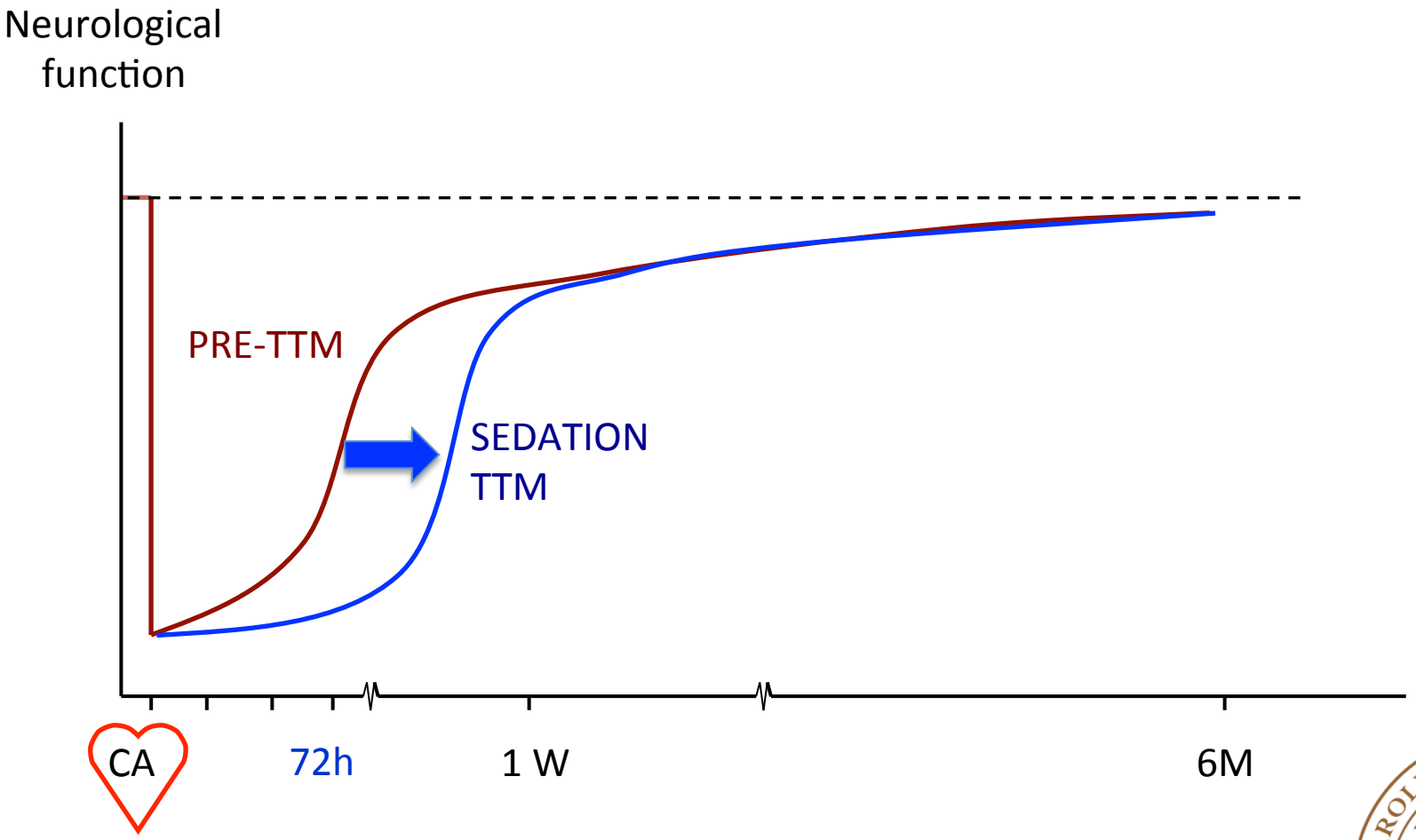
Pupillary reflex
Corneal reflex
Pain response

Vegetative state
Wakeful unresponsiveness

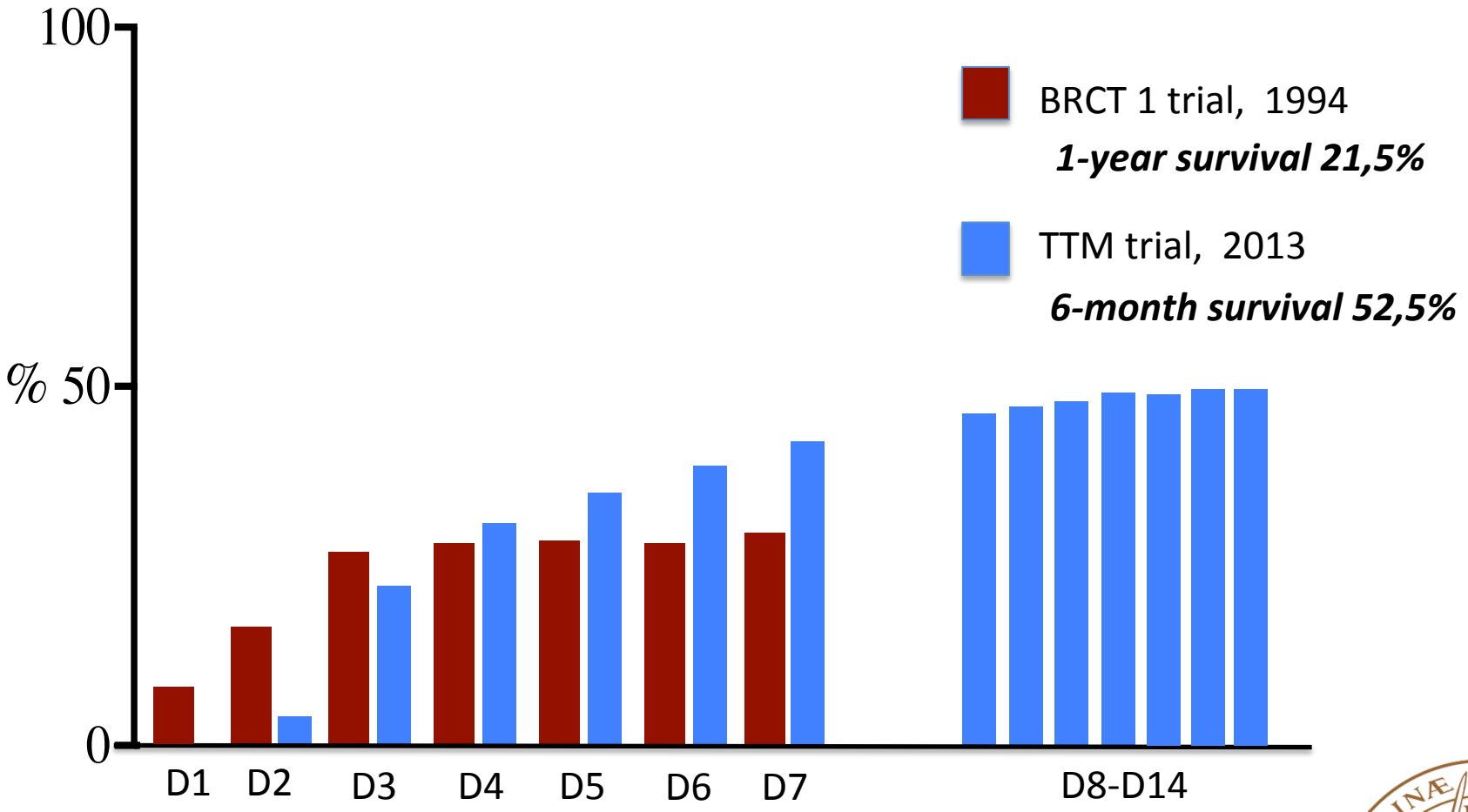
Modern intensive care makes clinical assessment more difficult and less reliable

- Targeted temperature management
- Pharmacological coma by sedative medication, analgesia and muscle relaxation
- Delayed metabolism of drugs
- Seizures may be masked

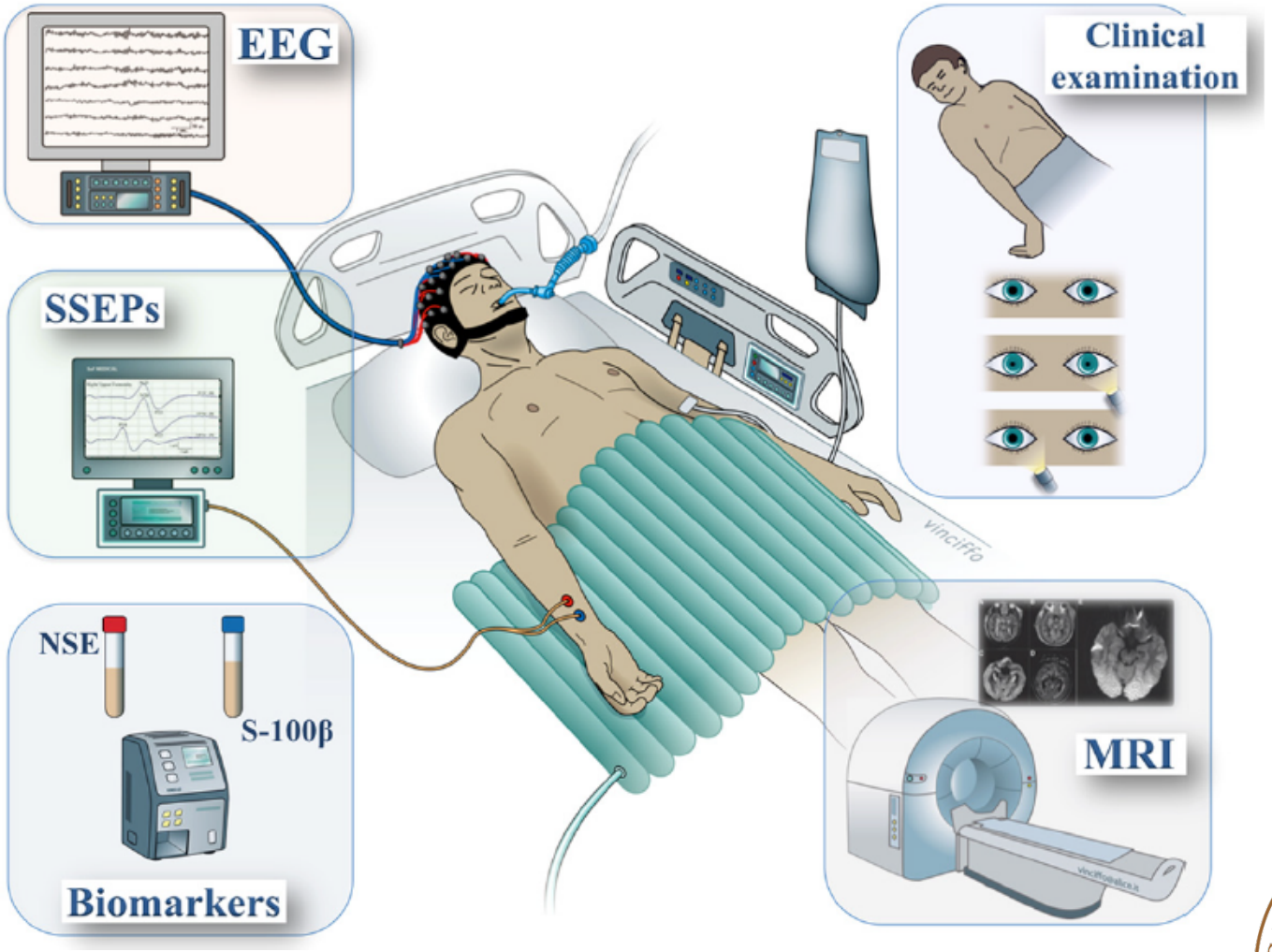
TTM may delay recovery for patients with good outcome



Awakening occurs later with TTM and sedation

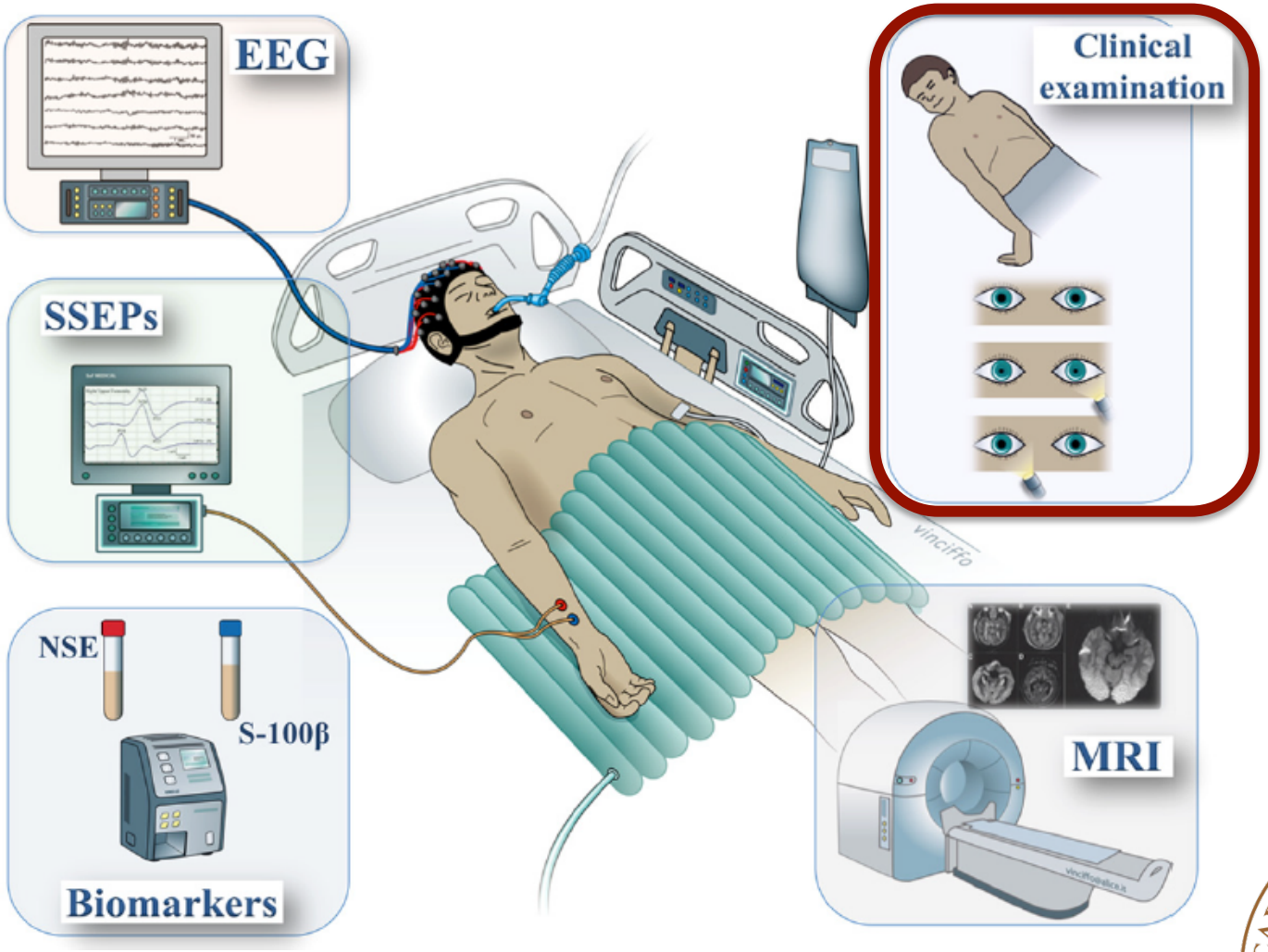


Neurological prognostication should be multimodal



Tacone, *Critical care*, 2014

Clinical examination is a central part



Tacone, *Critical care*, 2014

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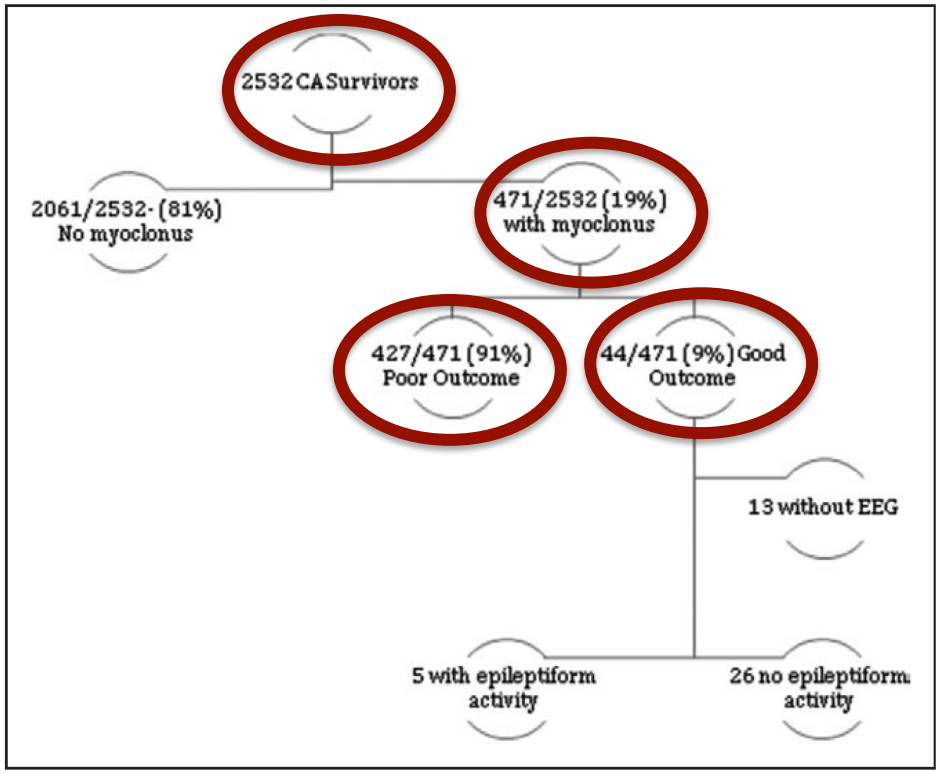
  - Tonus
  - Muscle stretch reflexes and plantar reflex

Prevalence of clinical seizures

INTCAR registry



Seder et al, *Crit Care Med*, 2015

Prevalence of clinical seizures

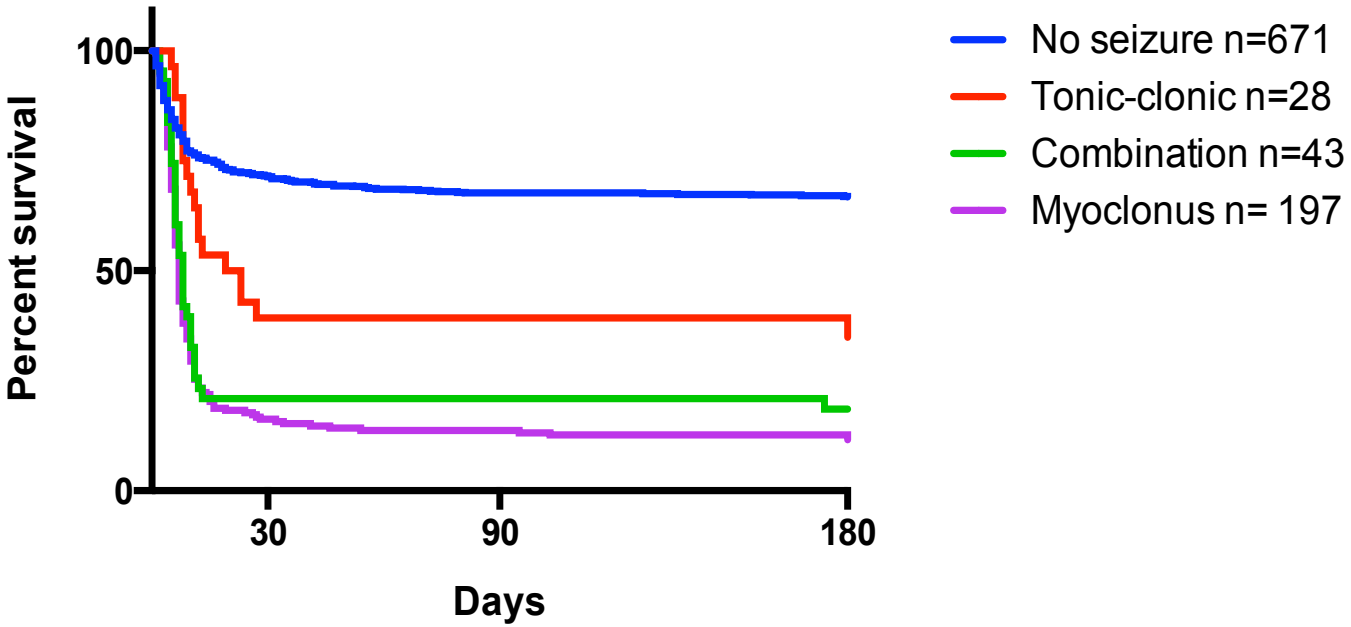
TTM trial

Table 2
Frequency of clinical seizures.

Seizure type	TTM33 (n = 473)	TTM36 (n = 466)	All (n = 939)
Any seizure	147 (31%)	121 (26%)	268 (29%)
Myoclonic	132 (28%)	108 (23%)	240 (26%)
Status myoclonus	37 (8%)	36 (8%)	73 (8%)
Focal myoclonus	48 (10%)	33 (7%)	81(8%)
Tonic-clonic	37 (8%)	34 (7%)	71 (8%)
Tonic-clonic status	12 (3%)	8 (2%)	20 (2%)
Focal tonic-clonic seizures	6 (1%)	5 (1%)	11 (1%)
Combination[a]	22 (5%)	21 (5%)	43(5%)

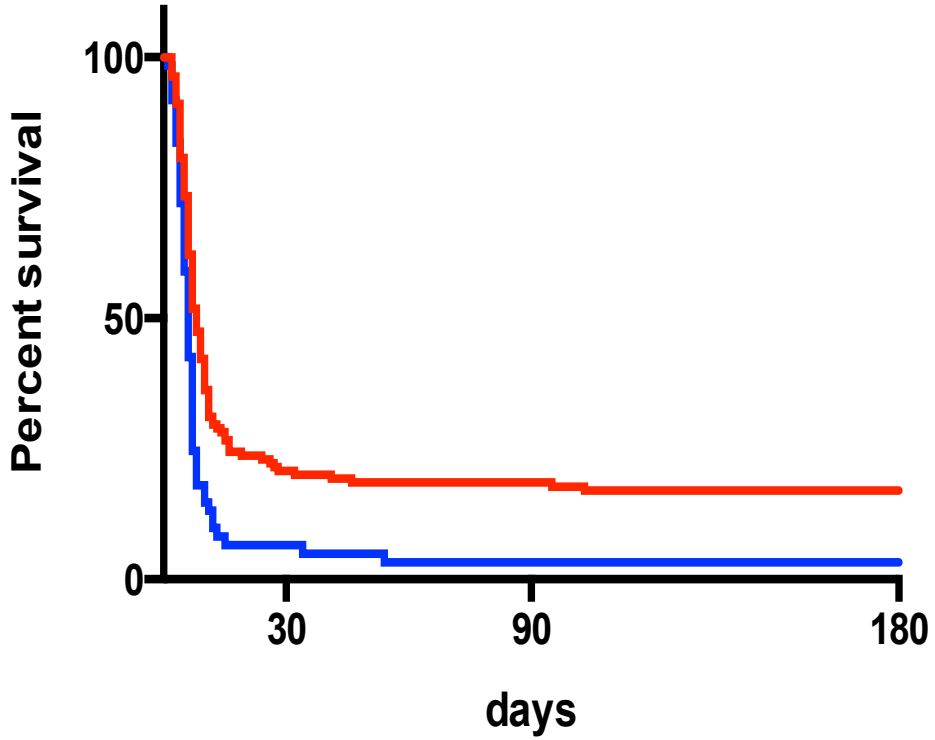
Lybeck, *Resuscitation*, 2017

Seizures are bad news



Lybeck, *Resuscitation*, 2017

Status myoclonus is **very** bad news



60/61 with status myoclonus had poor outcome

Lybeck, *Resuscitation*, 2017

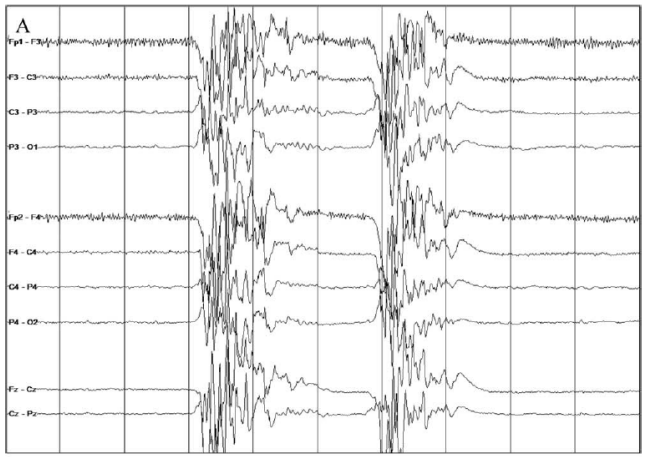
Clinically Distinct Electroencephalographic Phenotypes of Early Myoclonus after Cardiac Arrest

Jonathan Elmer, MD, MS,[1,2] Jon C. Rittenberger, MD, MS,[1] John Faro,[3]
Bradley J. Molyneaux, MD, PhD,[2,4] Alexandra Popescu, MD,[4]
Clifton W. Callaway, MD, PhD,[1] and Maria Baldwin, MD,[5]
for the Pittsburgh Post-Cardiac Arrest Service

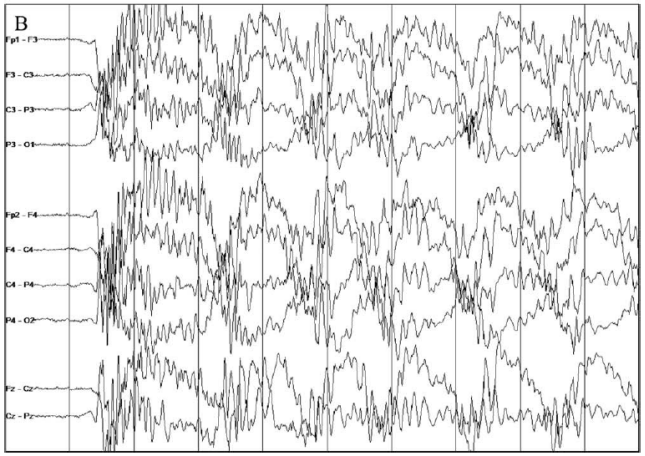
Objective: We tested the hypothesis that there are readily classifiable electroencephalographic (EEG) phenotypes of early postanoxic multifocal myoclonus (PAMM) that develop after cardiac arrest.
Methods: We studied a cohort of consecutive comatose patients treated after cardiac arrest from January 2012 to February 2015. For patients with clinically evident myoclonus before awakening, 2 expert physicians reviewed and classified all EEG recordings. Major categories included: Pattern 1, suppression-burst background with high-amplitude polyspikes in lockstep with myoclonic jerks; and Pattern 2, continuous background with narrow, vertex spike-wave discharges in lockstep with myoclonic jerks. Other patterns were subcortical myoclonus and unclassifiable. We compared population characteristics and outcomes across these EEG subtypes.
Results: Overall, 401 patients were included, of whom 69 (16%) had early myoclonus. Among these patients, Pattern 1 was the most common, occurring in 48 patients (74%), whereas Pattern 2 occurred in 8 patients (12%). The remaining patients had subcortical myoclonus (n = 2, 3%) or other patterns (n = 7, 11%). No patients with Pattern 1, subcortical myoclonus, or other patterns survived with favorable outcome. By contrast, 4 of 8 patients (50%) with Pattern 2 on EEG survived, and 4 of 4 (100%) survivors had favorable outcomes despite remaining comatose for 1 to 2 weeks postarrest.
Interpretation: Early PAMM is common after cardiac arrest. We describe 2 distinct patterns with distinct prognostic significances. For patients with Pattern 1 EEGs, it may be appropriate to abandon our current clinical standard of aggressive therapy with conventional antiepileptic therapy in favor of early limitation of care or novel neuroprotective strategies.

ANN NEUROL 2016;80:175–184

Type 1: Burst suppression with time-locked myoclonus

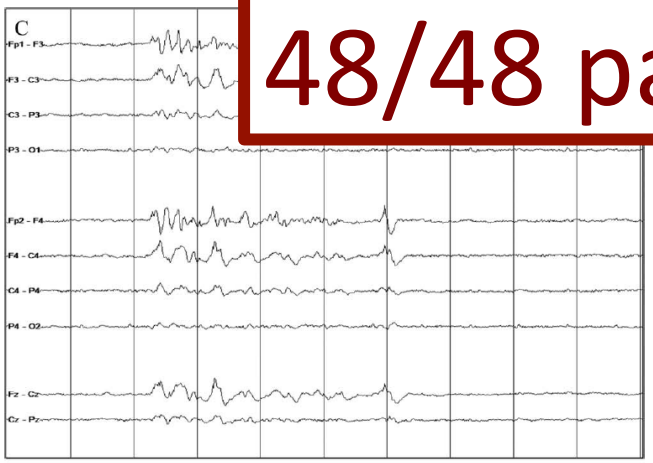


D0

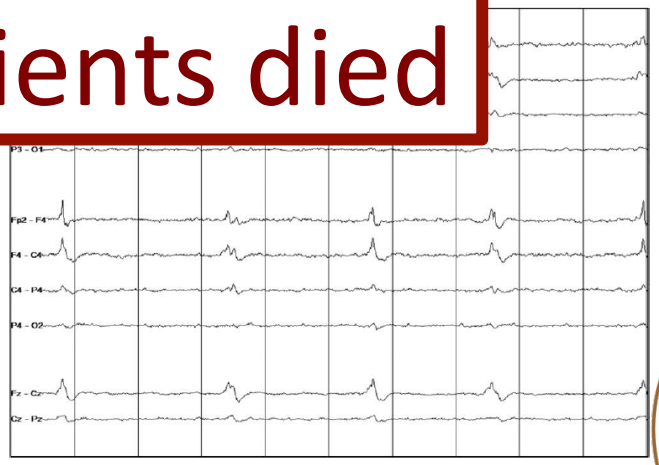


D1

48/48 patients died

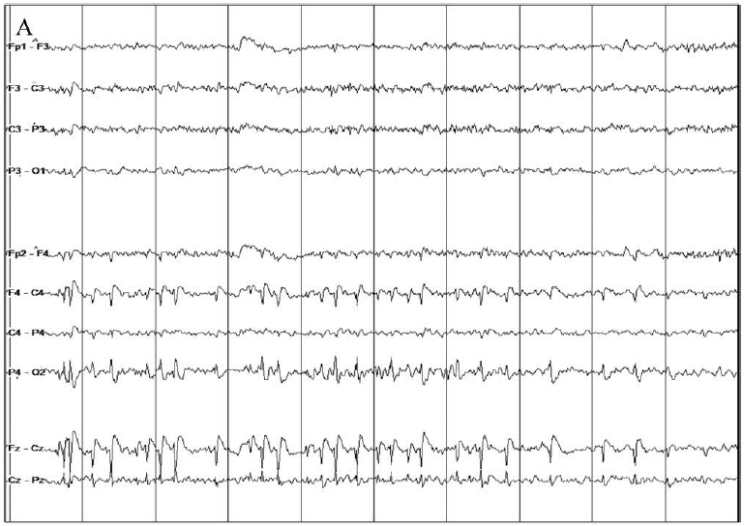


D2



D3

Type 2: Spike-wave with time-locked myoclonus



D0

D40

4/8 patients survived

All had Lance Adams action-myoclonus

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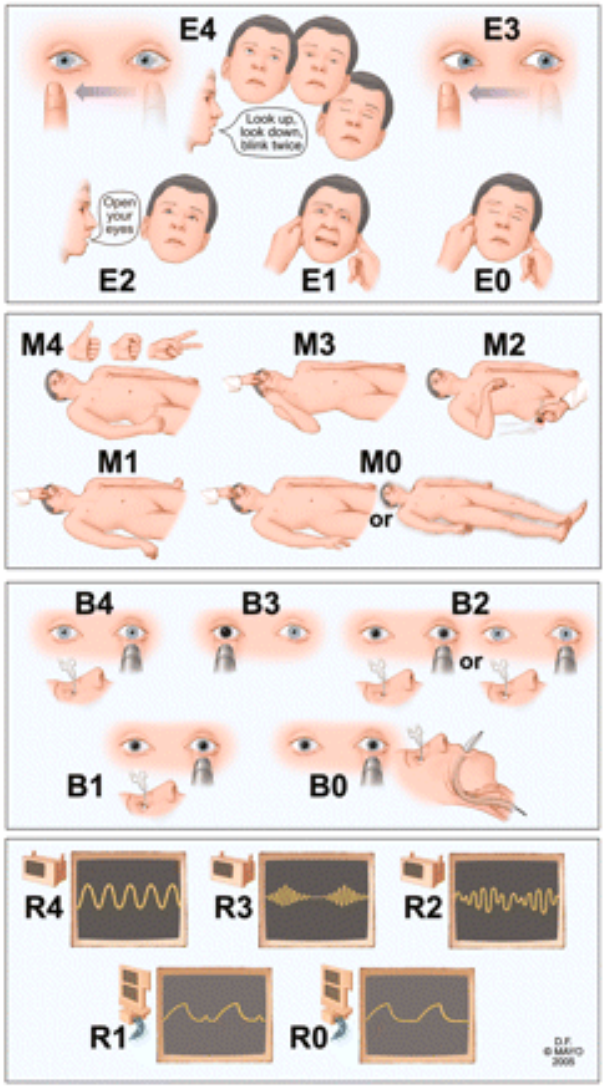
Glasgow coma scale

Teasdale and Jennet 1974

		Score
Eye opening	spontaneously	4
	to speech	3
	to pain	2
	none	1
Verbal response	orientated	5
	confused	4
	inappropriate	3
	incomprehensible	2
	none	1
Motor response	obeys commands	6
	localises to pain	5
	withdraws from pain	4
	flexion to pain	3
	extension to pain	2
	none	1
Maximum score		15

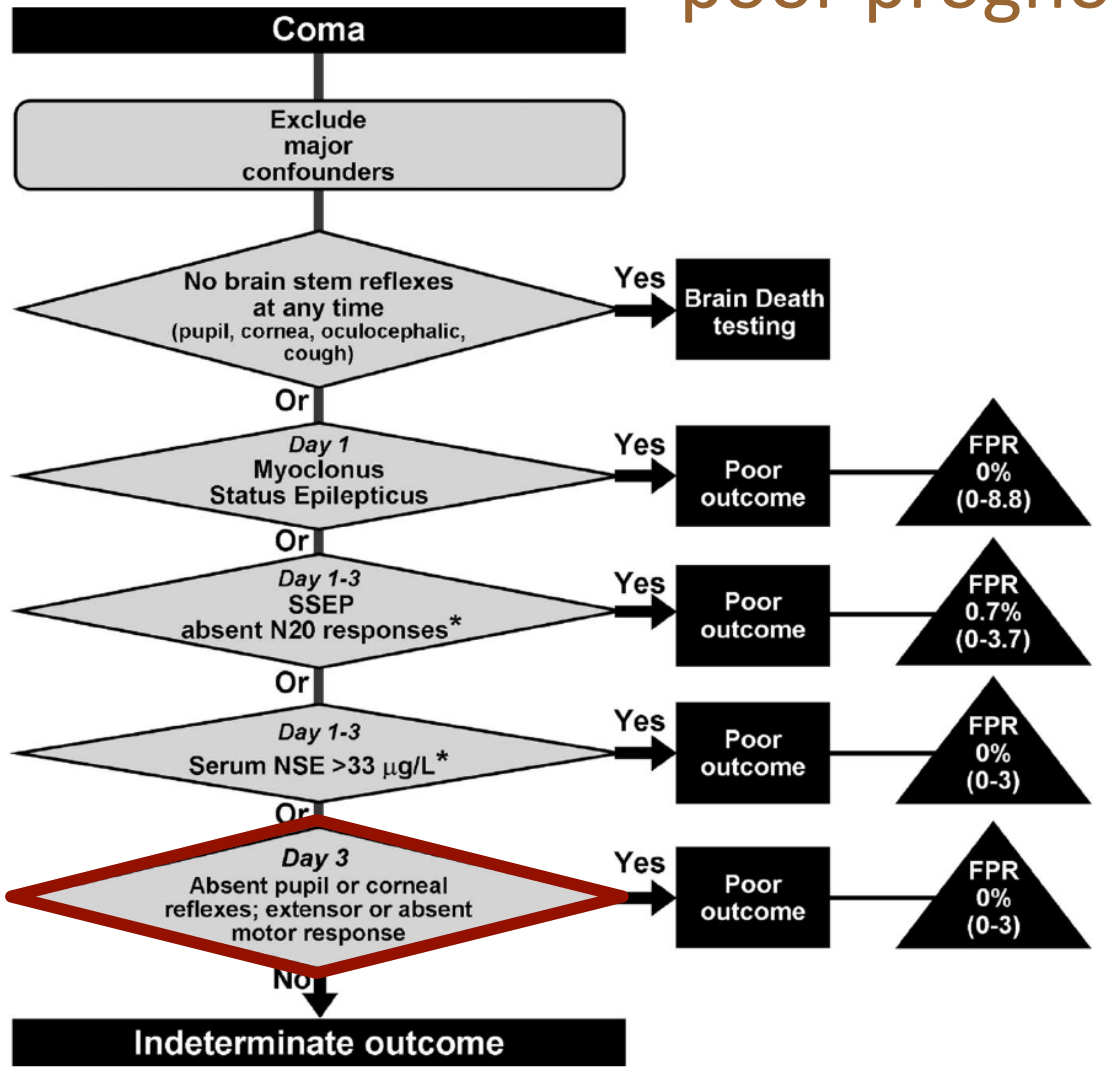
The FOUR-score



- Eye response
- Motor response
- Brainstem reflexes
- Respiration pattern

Wijdicks. *Ann Neurol.* 2005

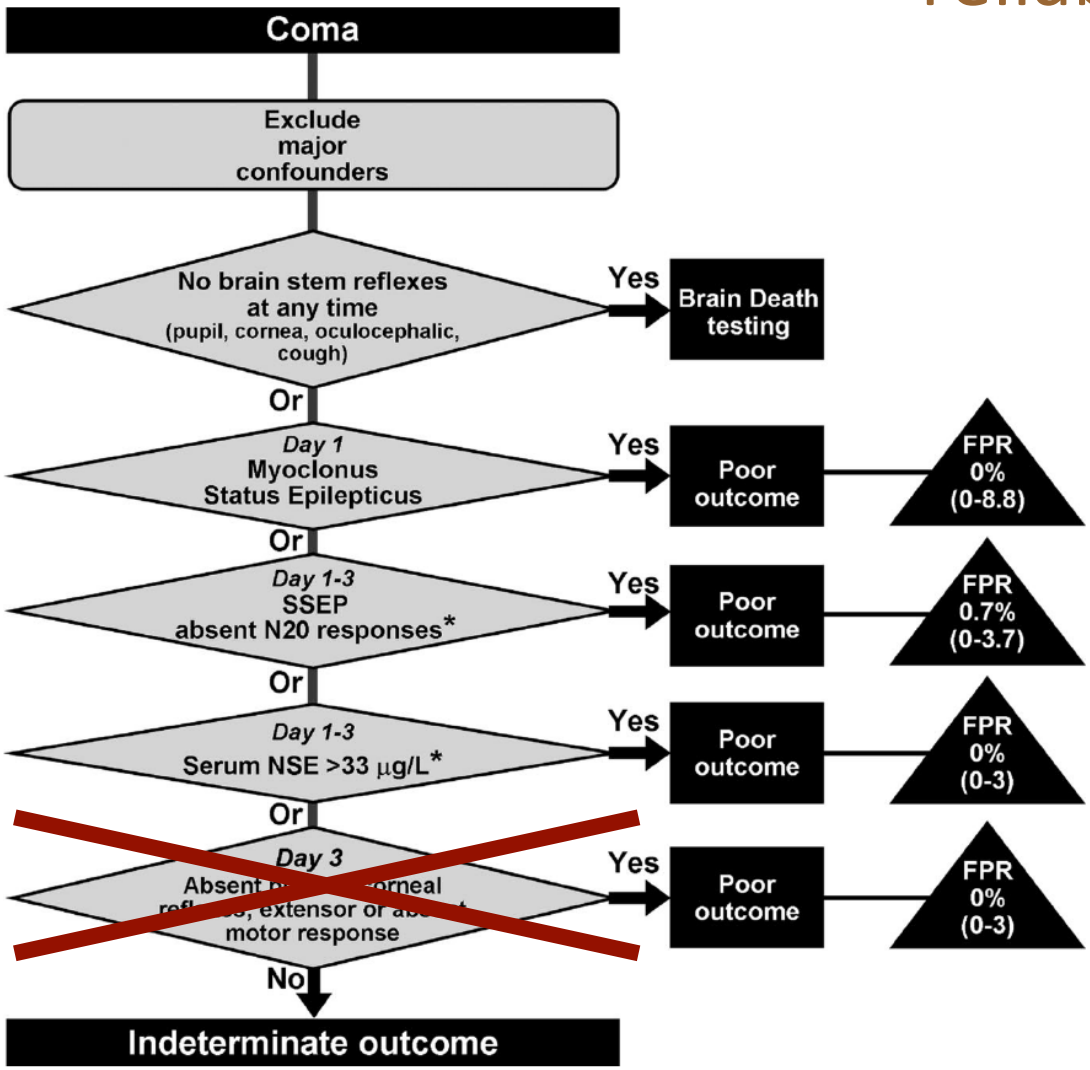
The AAN guidelines 2006 regarded extensor or absent motor response as a reliable sign of a poor prognosis



Levy, JAMA, 1985
Edgren, Lancet, 1994
Zandbergen, Neurology, 2006

Wijdicks, *Neurology*, 2006

In modern studies using temperature management and sedation absent motor response **is not** a reliable sign (FPR 10-24%)



Rossetti Ann Neurol, 2010(67)301-
Samaniego, Neurocrit Ca, 2011(15)
Bouwes, Ann Neurol, 2012(71)
Dragancea, Resuscitation, 2015

Wijdicks, *Neurology*, 2006

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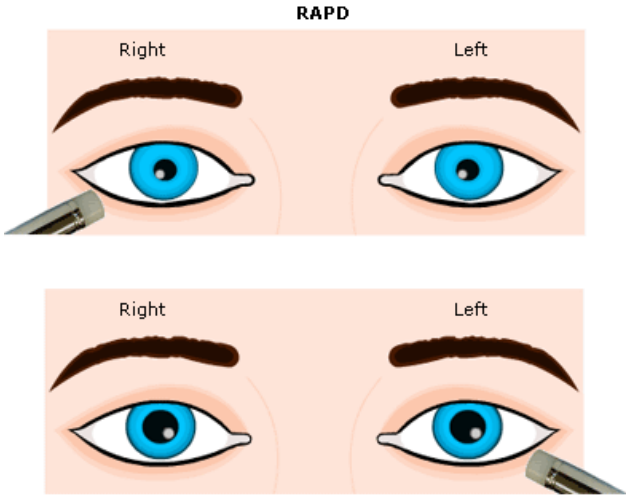
Bedside testing of brain stem function in the ICU

- Pupillary light reflex (N II,III)
- Corneal reflex (N V ,VII)
- Oculocephalic (Dolls eye) test / Oculovestibular reflex (cold water caloric test (N VIII, III, V))
- Gag and cough reflex (N IX, X)
- Spontaneous breathing pattern

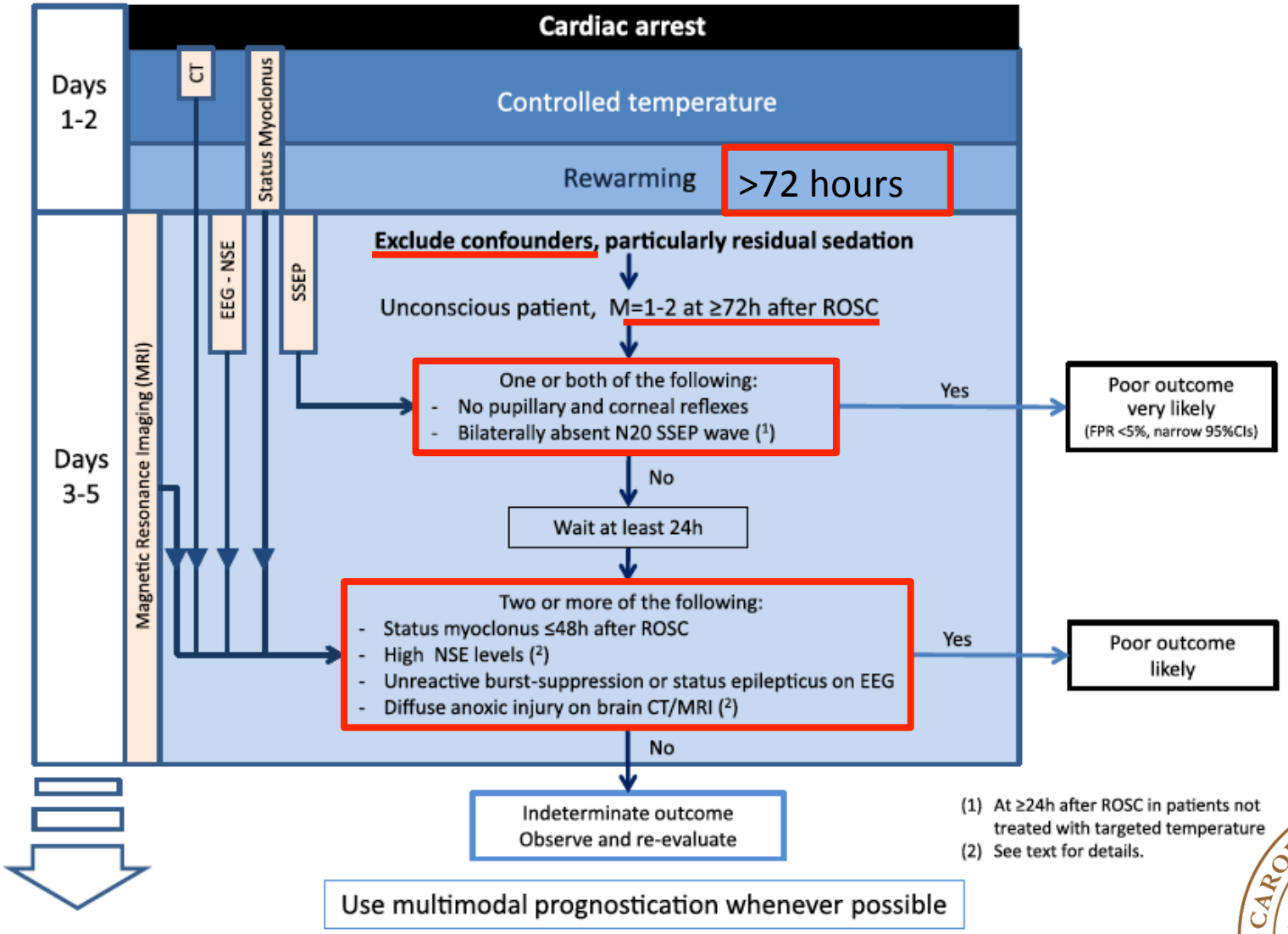
Bilateral absence of pupillary and corneal reflexes are reliable signs of a poor prognosis at 72 hours **BUT** with low sensitivity



test	TTM	sensitivity	FPR
PLR	no	18	0
-/-	yes	19	1
Corneal reflex	no	29	5
-/-	yes	26	4

Sandroni, resuscitation, 2014

European Recommendations



Sandroni. *ICM* 2014 *AND Nolan,* ERC/ESICM guidelines, Resuscitation and ICM 2015

Are we missing valuable bedside information from the PLR?

https://neuroptics.com/critical-care-info/

Automated infrared pupillometry

+

- High interrater reliability
- Improves sensitivity of the PLR in prognostication after CA
- Earlier detection of pupillary abnormalities in herniation/elevated ICP

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- Cost
- Risk of infection
- Need for training
- Not part of the guidelines

Pupillometry 48h after cardiac arrest

Author	n	Cut-off (%)	sensitivity(%)	specificity(%)
Suys, Neurocrit care, 2014*	50	13	61	100
Heimburger, Resuscitation, 2016	82	7	42	100
Solari, Ann Neurol, 2017*	103	13	63	100

Same device in all studies (NeuroLight, Algiscan)
* Same center, extended cohort

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Conclusions

- The combination of bilaterally absent pupillary light reflexes and corneal reflexes at 72h after CA is a reliable sign of poor prognosis.
- Absent or extensor motor response to pain is **not** a reliable sign of a poor prognosis at any time
- Seizures should always be considered in combination with EEG-information
- Pupillometry is a new and potentially useful tool that needs further validation in multi-center studies