

Case: 65 year old post-cardiac arrest patient with myoclonus

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Disclosures

- No financial conflicts of interest
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Case presentation (1)

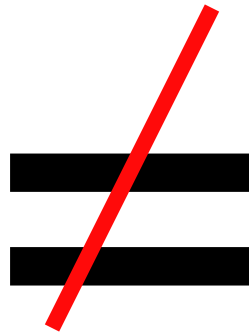


- 65 yo man collapsed at baseball game
 - 26 minutes CPR, VF, defibrillation x 4, epinephrine x 3mg, intubated in field
 - In ED flaccid, CVC placed, NE initiated
 - In ICU
 - MAP 70-100, PaO₂ 207, pCO₂ 44, glc 145
 - Continuous, slow EEG background, occasional PEDs
 - About 11 hours into TTM at 33C, facial twitch, then generalized jerking movements

Case presentation (2)



- 65 yo man collapsed at baseball game
 - 26 minutes CPR, VF, defibrillation x 4, epinephrine x 3mg, intubated in field
 - In ED flaccid, hypotensive, acidotic
 - In ICU
 - MAP 50, PaO₂ 407, pCO₂ 29, glc 345
 - Flat EEG background, occasional PEDs
 - About 11 hours into TTM at 33C, facial twitch, then generalized jerking movements



Myoclonus

- “Brief, involuntary twitching of a muscle or a group of muscles
- All myoclonus is not seizure, and all seizure is not myoclonus

Early EEG correlates of neuronal injury after brain anoxia

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ABSTRACT

Objectives: EEG and serum neuron-specific enolase (NSE) are used for outcome prognostication in patients with postanoxic coma; however, it is unclear if EEG abnormalities reflect transient neuronal dysfunction or neuronal death. To assess this question, EEG abnormalities were correlated with NSE. Moreover, NSE cutoff values and hypothermic EEG features related with poor outcome were explored.

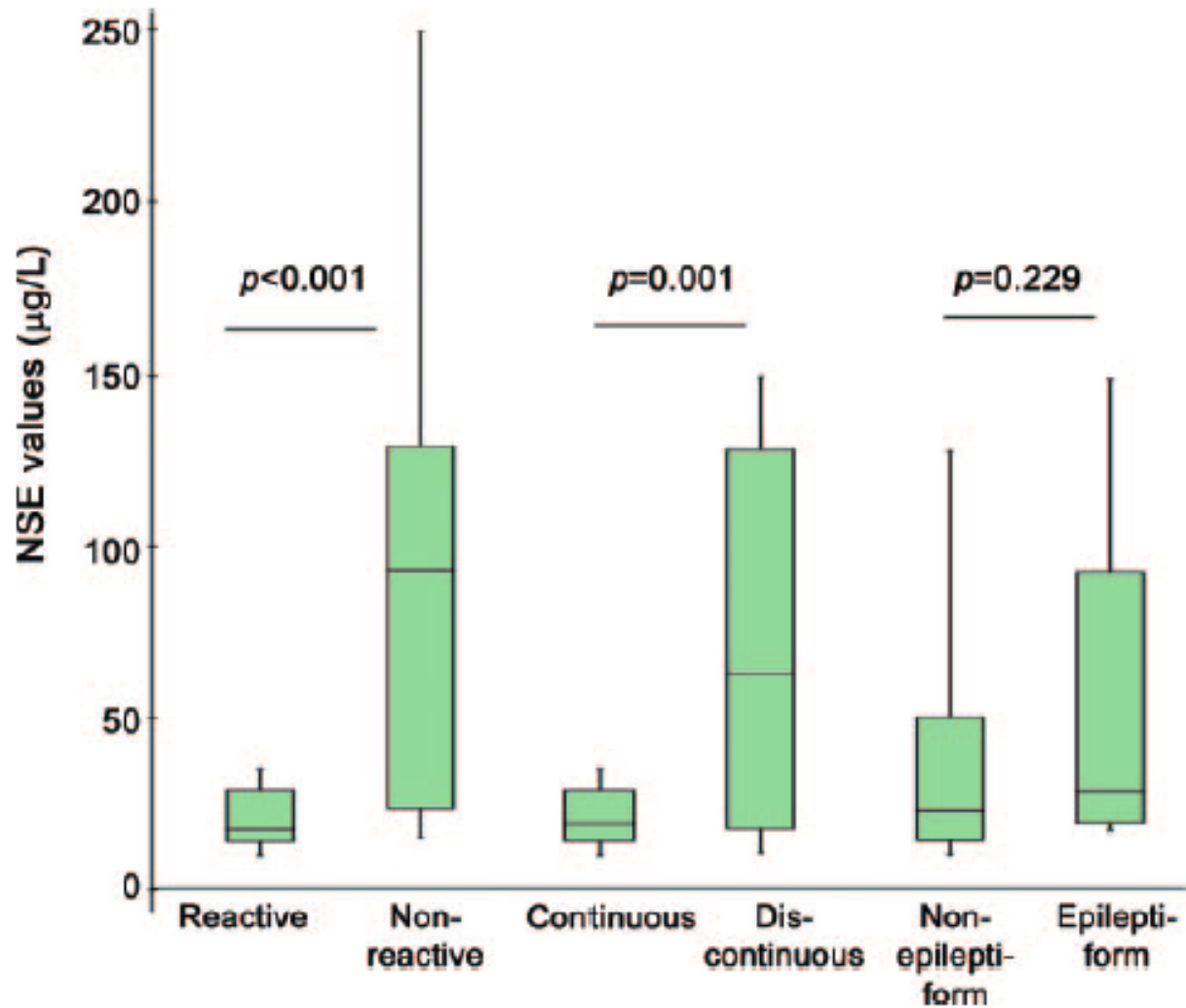
Methods: In a prospective cohort of 61 adults treated with therapeutic hypothermia (TH) after cardiac arrest (CA), multichannel EEG recorded during TH was assessed for background reactivity and continuity, presence of epileptiform transients, and correlated with serum NSE collected at 24–48 hours after CA. Demographic, clinical, and functional outcome data (at 3 months) were collected and integrated in the analyses.

Results: In-hospital mortality was 41%, and 82% of survivors had good neurologic outcome at 3 months. Serum NSE and EEG findings were strongly correlated (Spearman rho = 0.45; $p < 0.001$). Median NSE peak values were higher in patients with unreactive EEG background ($p < 0.001$) and discontinuous patterns ($p = 0.001$). While all subjects with nonreactive EEG died, 5 survivors (3 with good outcome) had NSE levels $>33 \mu\text{g/L}$.

Conclusion: The correlation between EEG during TH and serum NSE levels supports the hypothesis that early EEG alterations reflect permanent neuronal damage. Furthermore, this study confirms that absent EEG background reactivity and presence of epileptiform transients are robust predictors of poor outcome after CA, and that survival with good neurologic recovery is possible despite serum NSE levels $> 33 \mu\text{g/L}$. This underscores the importance of multimodal assessments in this setting. *Neurology*® 2012;78:796–802

Figure

Associations between serum neuron-specific enolase (NSE) and EEG during therapeutic hypothermia



Predictors of awakening from postanoxic status epilepticus after therapeutic hypothermia

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ABSTRACT

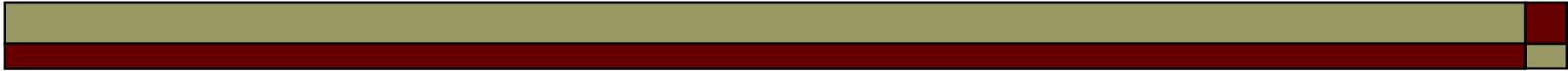
Background: Postanoxic status epilepticus (PSE) is considered a predictor of fatal outcome and therefore not intensively treated; however, some patients have had favorable outcomes. The aim of this study was to identify favorable predictors for awakening beyond vegetative state in PSE.

Methods: We studied six subjects treated with hypothermia improving beyond vegetative state after cerebral anoxia, despite PSE. They were among a cohort of patients treated for anoxic encephalopathy with therapeutic hypothermia in our institution between October 1999 and May 2006 (retrospectively, 3/107 patients) and June 2006 and May 2008 (prospectively, 3/74 patients). PSE was defined by clinical and EEG criteria. Outcome was assessed according to the Glasgow-Pittsburgh Cerebral Performance Categories (CPC).

Results: All improving patients had preserved brainstem reflexes, cortical somatosensory evoked potentials, and reactive EEG background during PSE. Half of them had myoclonic PSE, while three had nonconvulsive PSE. In the prospective arm, 3/28 patients with PSE showed this clinical-electrophysiologic profile; all awoke. Treatments consisted of benzodiazepines, various antiepileptic drugs, and propofol. One subject died of pneumonia in a minimally conscious state, one patient returned to baseline (CPC1), three had moderate impairment (CPC2), and one remained dependent (CPC3). Patients with nonconvulsive PSE showed a better prognosis than subjects with myoclonic PSE ($p = 0.042$).

Conclusion: Patients with postanoxic status epilepticus and preserved brainstem reactions, somatosensory evoked potentials, and EEG reactivity may have a favorable outcome if their condition is treated as status epilepticus. *Neurology*® 2009;72:744-749

	Retrospective	Retrospective	Retrospective	Prospective	Prospective	Prospective	
Data collection	Retrospective	Retrospective	Retrospective	Prospective	Prospective	Prospective	
Age, y	60	61	55	53	68	58	53-6
Female	Yes	Yes	No	No	No	No	2/4
CA due to VF	Yes	Yes	No	Yes	Yes	Yes	5/6
Time to ROSC, min	32	45	17	20	20	21	17-4
Cardiac etiology	Yes	Yes	Yes	Yes	Yes	Yes	6/6*
Preserved BR	Yes	Yes	NA	Yes	Yes	Yes	5/5*
Absent MR	Yes	No	NA	No	No	Yes	2/5
SE diagnosis delay from CA, d	2	4	2	2	3	9	2-9
SE clinically (myoclonus)	Yes	No	Yes	Yes	No	No	3/6
EEG description	Repetitive diffuse sharp waves (1.5 Hz), bilateral	Repetitive diffuse sharp waves (2-3 Hz), bilateral	Repetitive diffuse sharp waves (2 Hz), bilateral	Sharp waves, spike-waves (2 Hz), L>R; SIRPID	Frontal evolving rhythmic sharp waves (3 Hz), bilateral	Frontal poly-spike-waves (2-3 Hz), R>L	
EEG reactivity	Yes	Yes	Yes	Yes	Yes	Yes	6/6*
PSE duration (d, on EEG)	3	2	2	2	5	3	2-5
Preserved N20 on SSEP	Yes	NA	Yes	Yes	Yes	Yes	5/5*
AEDs	PRO. VPA.	VPA. CLZ.	PRO. PHT.	VPA. PHT.	PRO. VPA.	VPA. LEV.	



Neurologic Outcomes and Postresuscitation Care of Patients With Myoclonus Following Cardiac Arrest*

David B. Seder, MD¹; Kjetil Sunde, MD, PhD²; Sten Rubertsson, MD³; Michael Mooney, MD²; Pascal Stammet, MD⁴; Richard R. Riker, MD¹; Karl B. Kern, MD⁵; Barbara Unger, RN⁶; Tobias Cronberg, MD⁷; John Dziodzio, BA¹; Niklas Nielsen, MD, PhD^{7,8}; for the International Cardiac Arrest Registry

Objectives: To evaluate the outcomes of cardiac arrest survivors with myoclonus receiving modern postresuscitation care.
Design: Retrospective review of registry data.
Setting: Cardiac arrest receiving centers in Europe and the United States from 2002 to 2012.
Patients: Two thousand five hundred thirty-two cardiac arrest survivors 18 years or older enrolled in the International Cardiac Arrest Registry.
Interventions: None.
Measurements and Main Results: Eighty-eight percent of patients underwent therapeutic hypothermia and 471 (18%) exhibited myoclonus. Patients with myoclonus had longer time to professional cardiopulmonary resuscitation (8.6 vs 7.0 min; $p < 0.001$) and total ischemic time (25.6 vs 22.3 min; $p < 0.001$) and less

often presented with ventricular tachycardia/ventricular fibrillation, a witnessed arrest, or had bystander cardiopulmonary resuscitation. Electroencephalography demonstrated myoclonus with epileptiform activity in 209 of 374 (55%), including status epilepticus in 102 of 374 (27%). Good outcome (Cerebral Performance Category 1–2) at hospital discharge was noted in 9% of patients with myoclonus, less frequently in myoclonus with epileptiform activity (2% vs 15%; $p < 0.001$). Patients with myoclonus with good outcome were younger (53.7 vs 62.7 yr; $p < 0.001$), had more ventricular tachycardia/ventricular fibrillation (81% vs 46%; $p < 0.001$), shorter ischemic time (18.9 vs 26.4 min; $p = 0.003$), more witnessed arrests (91% vs 77%; $p = 0.02$), and fewer “do-not-resuscitate” orders (7% vs 78%; $p < 0.001$). Life support was withdrawn in 330 of 427 patients (78%) with myoclonus and poor outcome, due to neurological futility in 293 of 330 (89%), at 5 days (3–8 d) after resuscitation. With myoclonus and good outcome, median ICU length of stay was 8 days (5–11 d) and hospital length of stay was 14.5 days (9–22 d).

Conclusions: Nine percent of cardiac arrest survivors with myoclonus after cardiac arrest had good functional outcomes, usually in patients without associated epileptiform activity and after prolonged hospitalization. Deaths occurred early and primarily after withdrawal of life support. It is uncertain whether prolonged care would yield a higher percentage of good outcomes, but myoclonus of itself should not be considered a sign of futility. (*Crit Care Med* 2015; 43:965–972)

Key Words: arrest; cardiac; myoclonic; myoclonus; seizure; status epilepticus

*See also p. 1136.
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⁸Department of Anesthesia and Intensive Care, Helsingborg Hospital, Helsingborg, Sweden.
Dr. Sunde received payment for lectures and travel grants from Bard Medical and Saint Medical Group, Thailand (both companies manufac-

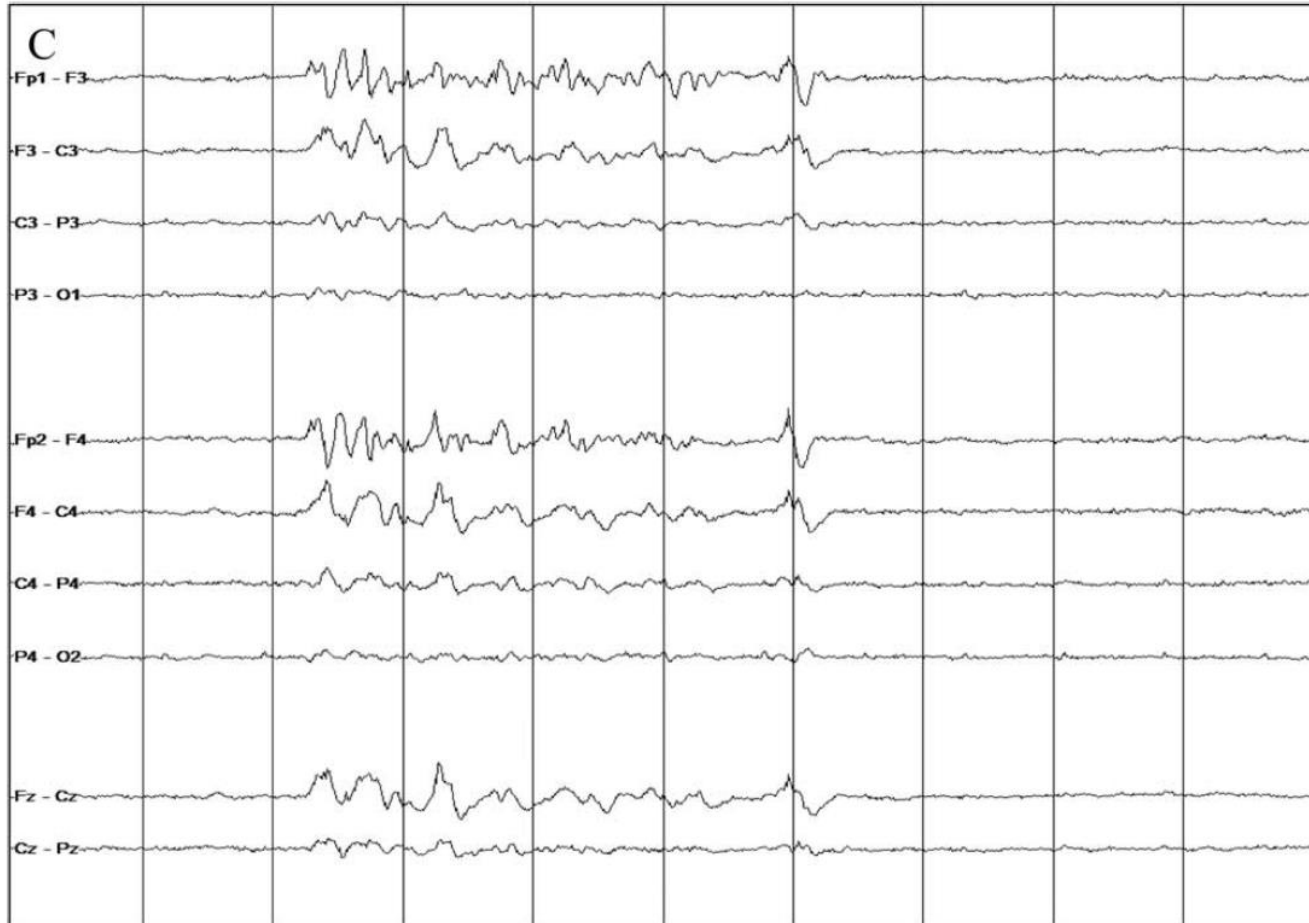
- ❑ Large registry data set
- ❑ 18% myoclonus
- ❑ Of those, 9% GNO at 6mo
- ❑ Better outcomes when myoclonus did not have an EEG correlate (15% v 2%)

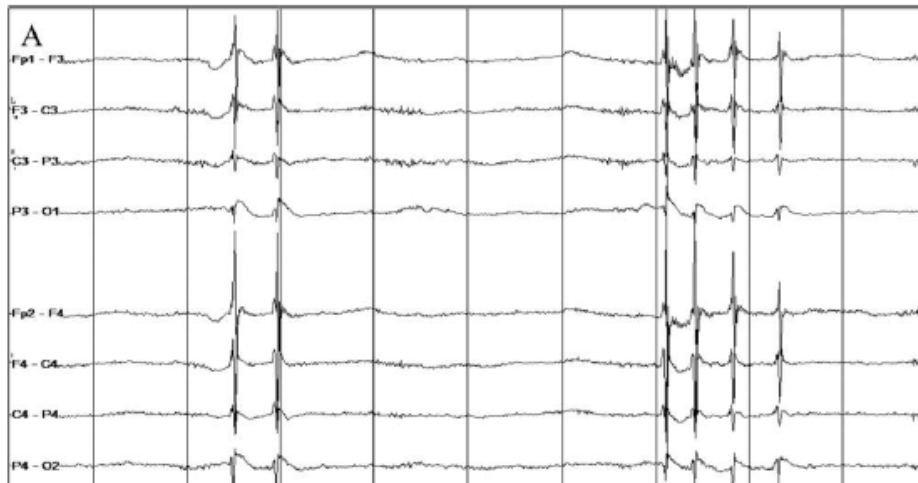


Myoclonus...

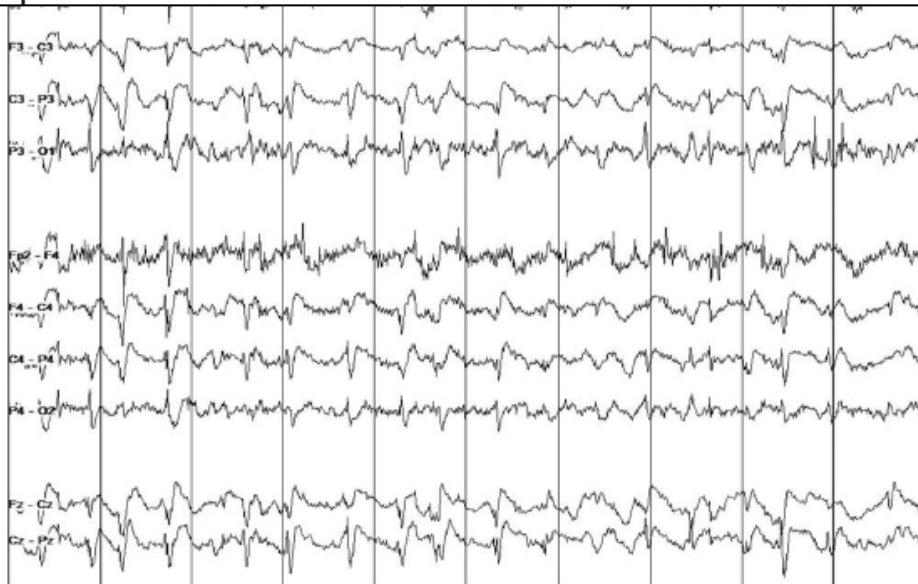
- Patients with GNO had ~15 days ICU stay
- Patients with PNO had ~5 day ICU stay
- Patients with PNO routinely had early WLST
- Unclear how many patients with myoclonus would have survived if therapy continued

Myoclonus SE subtypes?





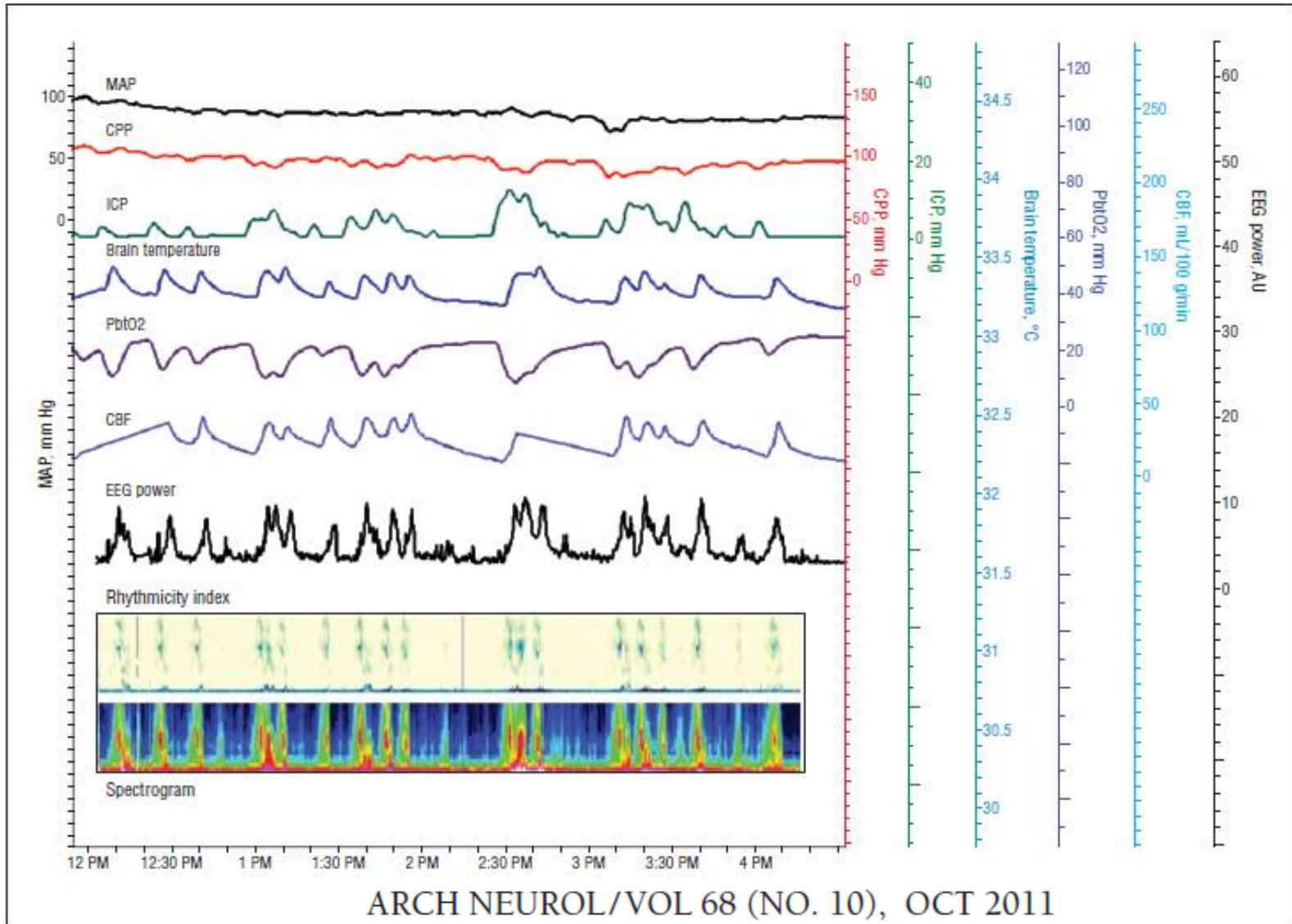
Results: Overall, 401 patients were included, of whom 69 (16%) had early myoclonus. Among these patients, Pattern 1 was the most common, occurring in 48 patients (74%), whereas Pattern 2 occurred in 8 patients (12%). The remaining patients had subcortical myoclonus (n = 2, 3%) or other patterns (n = 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.



Ann Neurol. 2016 Aug;80(2):175-84.

Status Epilepticus–Induced Hyperemia and Brain Tissue Hypoxia After Cardiac Arrest

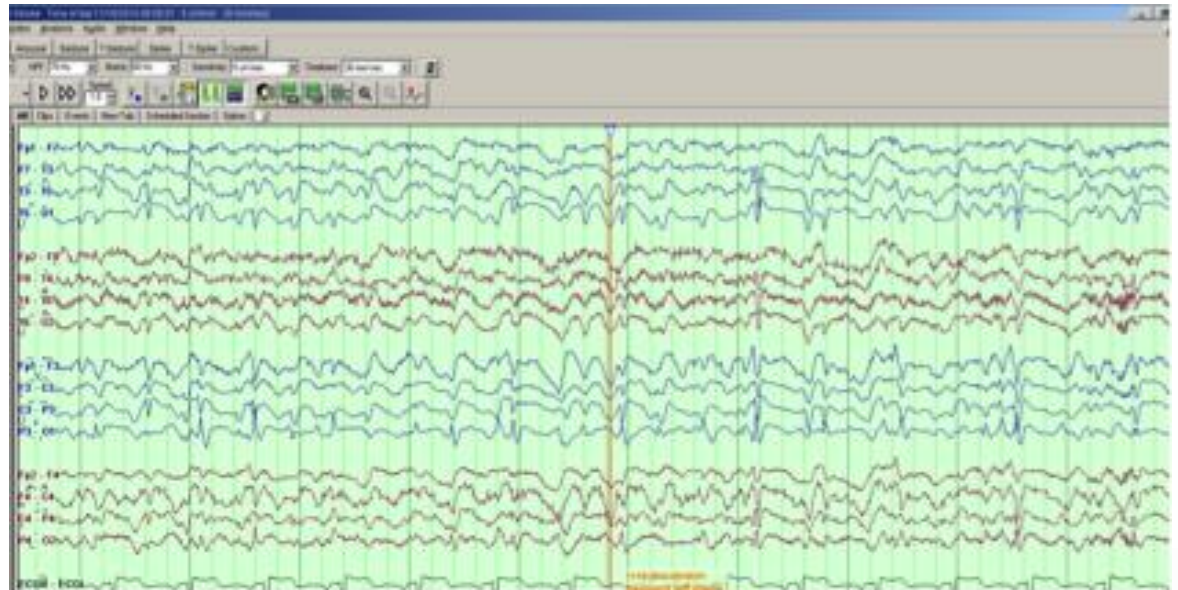
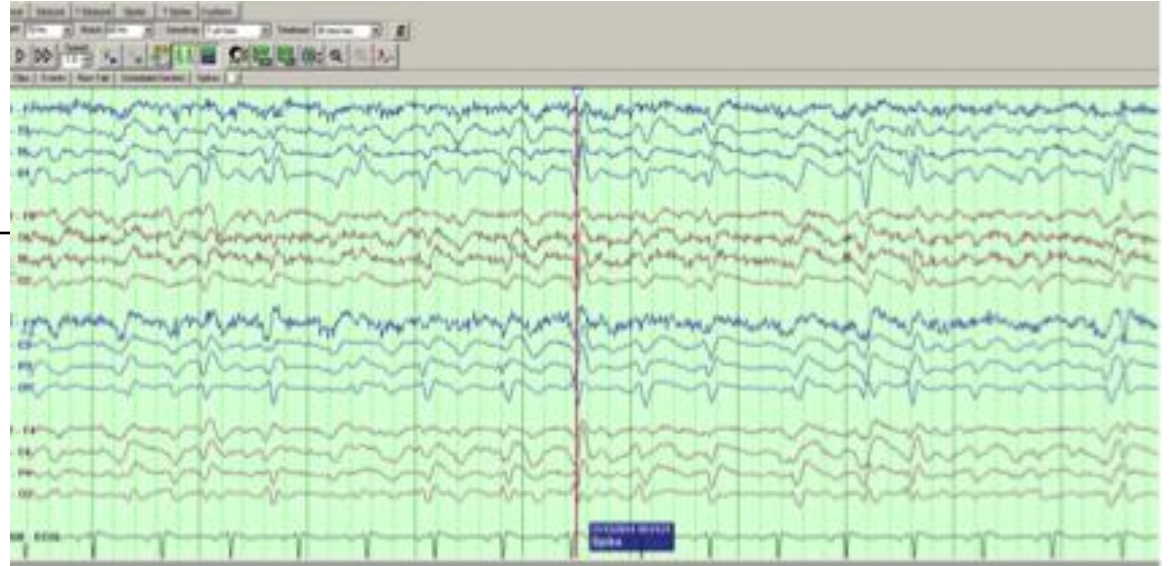
Sang-Bae Ko, MD, PhD; Santiago Ortega-Gutierrez, MD; H. Alex Choi, MD; Jan Claassen, MD, PhD; Mary Presciutti, RN; J. Michael Schmidt, PhD; Neeraj Badjatia, MD, MS; Kiwon Lee, MD; Stephan A. Mayer, MD



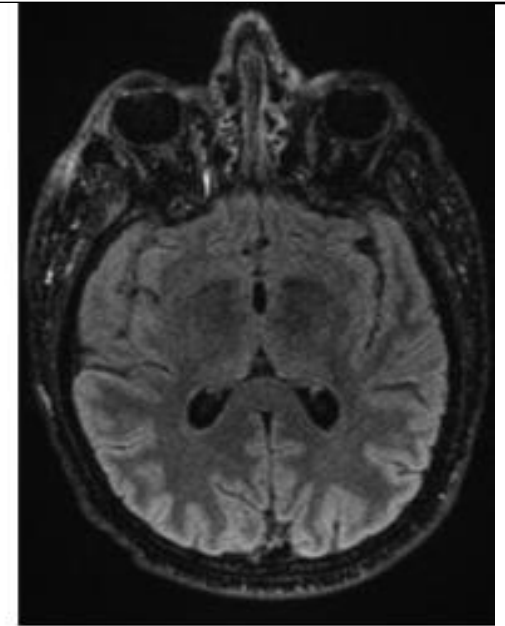
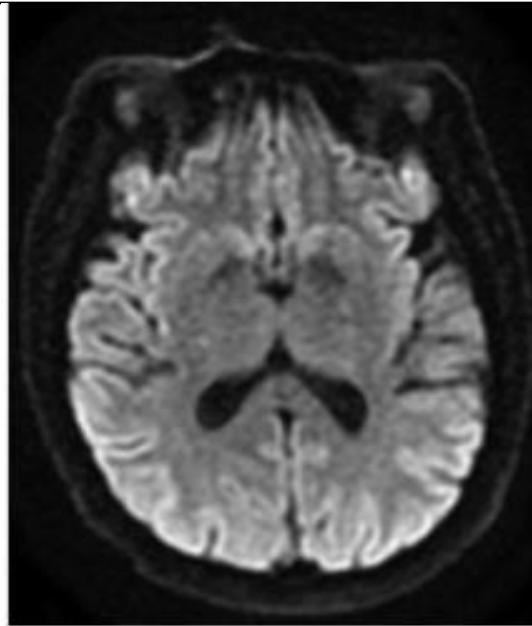
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- 54 year-old man separated two fighting dogs, was bitten on the arm, and collapsed pulseless and apneic in the snow
 - Bystander CPR was initiated and when EMS arrived the initial heart rhythm was VF
 - STEMI, Cath, LAD stent and GCS 5 on arrival to CICU

-
- Therapeutic hypothermia to 33° C was initiated
 - Severe myoclonus and epileptiform activity developed, and 33C prolonged to 60 hours
 - NSE peak was 35 ng/ml at 48 hours
 - He exhibited severe whole-body jerking starting about 12 hours after ROSC, worse after stimulation

- EEG showed GPEDS and then PLEDs evolving from a slowed background
- There are periods of PLEDS and GPEDS > 1 Hz



- Modest DWI injury
- Prolonged therapy with slow wean of sedating AEDs

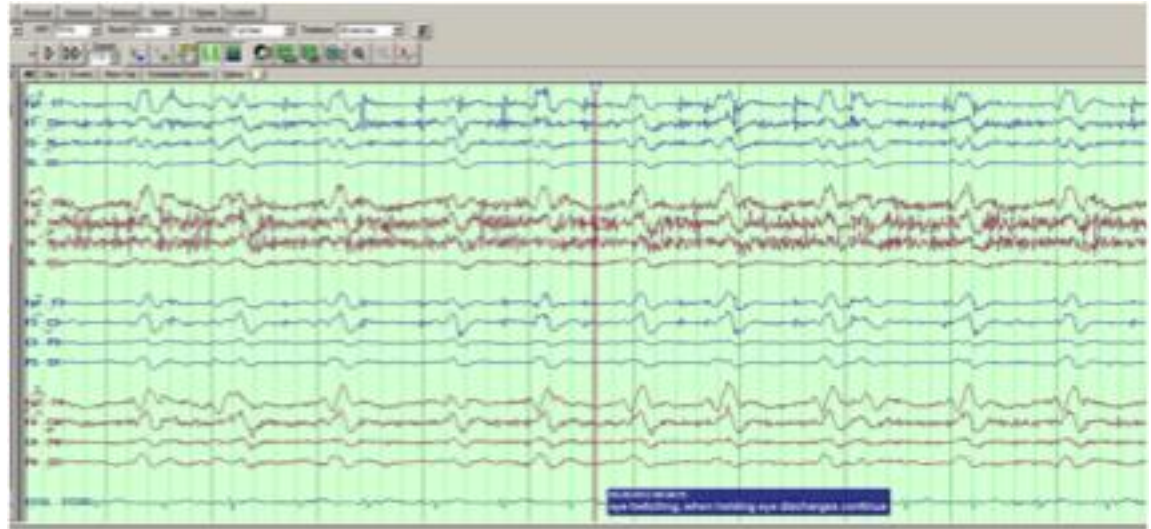


DWI and FLAIR MRI sequences performed 82 hours after ROSC. There is no appreciable injury to cortex or deep gray matter structures

-
- Levitiracetam, valproate, and BDZ
 - Followed commands and extubated on day #12
 - Interactive, ambulatory with assistance, taking a full diet, and participating in therapy activities on post-arrest day #20
 - Discharged to acute inpatient rehabilitation: 90% independent in ADLs at 60 days post-arrest
 - “Who is this Dr. Fahrenbach? What is the appointment for?”

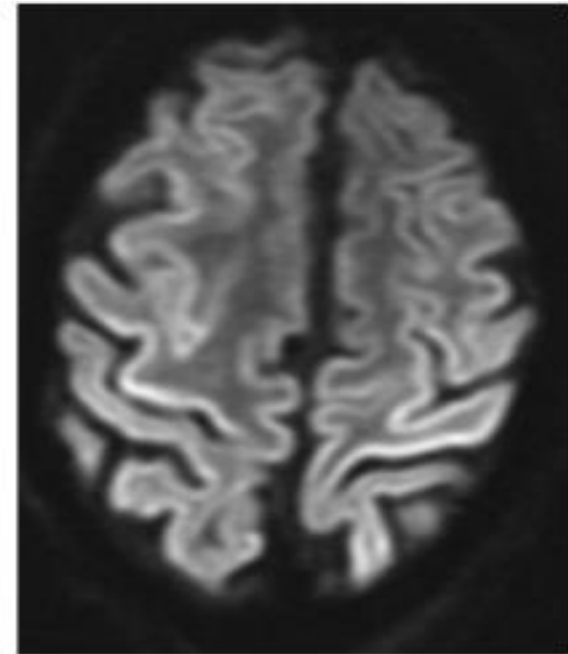
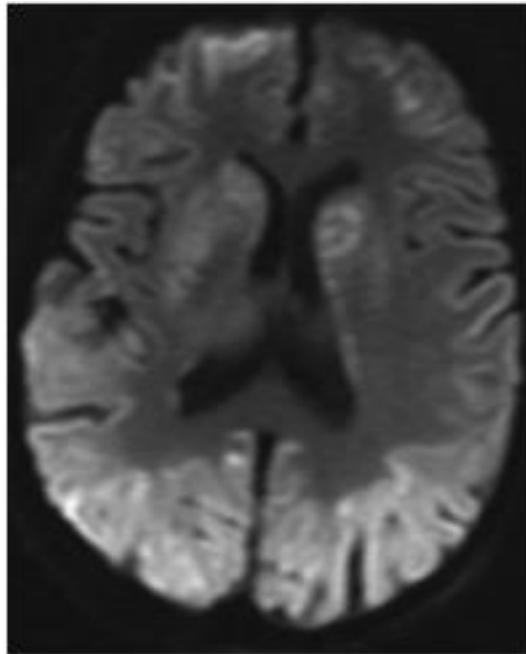
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- 74 yo woman with COPD and h/o anal carcinoma was found unresponsive by her husband
 - On EMS arrival, the rhythm was PEA
 - CPR initiated and ROSC occurred with Epi 1mg x 2
 - Underwent hypothermia to 33C x 24 hours

- Myoclonic twitching developed during rewarming the involving eyes and face



GPEDS evolved from a burst-suppression background, and correlated with eye twitching

-
- Diffuse and severe injury: MRI shows cortical ribboning c/w laminar necrosis



MRI showing abnormal cortical DWI with an occipital and frontal predominance

-
- NSE peak was 282 ng/mL
 - Physical examination on hospital day #3 showed GCS 3, intact corneal. oculocephalic, and pupillary reflexes, and spontaneous respiration present
 - Life support was withdrawn at family request, and she died 102 hours post-arrest.

-
- 19 ♀ OHCA d/t Status Asthmaticus – ischemic time ~20 minutes
 - Initially reactive EEG background, then developed EDs and suppression
 - Hemodynamically stable – cooled to 33C x 24h

-
- Myoclonus, then super refractory status epilepticus
 - MRI normal, 72h NSE level 14ng/dL
 - Maintained at 35C x 5 days for ongoing SZ
 - Pentobarbital coma, 8 AEDs

-
- Gradual recovery complicated by Lance-Adams syndrome, trach decannulated on HD 33, severe debility
 - Discharged HD 58 to acute inpatient rehab
 - Excellent cognitive recovery – personality and intelligence intact
 - Severe intention myoclonus on most recent evaluation
 - PEG tube, aspiration issues, inpatient facility



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Prognostication in comatose survivors of cardiac arrest: An advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine[☆]



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ABSTRACT

Objectives: To review and update the evidence on predictors of poor outcome (death, persistent vegetative state or severe neurological disability) in adult comatose survivors of cardiac arrest, either treated or not treated with controlled temperature, to identify knowledge gaps and to suggest a reliable prognostication strategy.

Methods: GRADE-based systematic review followed by expert consensus achieved using Web-based Delphi methodology, conference calls and face-to-face meetings. Predictors based on clinical examination, electrophysiology, biomarkers and imaging were included.

Results and conclusions: Evidence from a total of 73 studies was reviewed. The quality of evidence was low or very low for almost all studies. In patients who are comatose with absent or extensor motor response at ≥ 72 h from arrest, either treated or not treated with controlled temperature, bilateral absence of either pupillary and corneal reflexes or N20 wave of short-latency somatosensory evoked potentials were identified as the most robust predictors. Early status myoclonus, elevated values of neuron specific enolase at 48–72 h from arrest, unreactive malignant EEG patterns after rewarming, and presence of diffuse signs of postanoxic injury on either computed tomography or magnetic resonance imaging were identified as useful but less robust predictors. Prolonged observation and repeated assessments should be considered when results of initial assessment are inconclusive. Although no specific combination of predictors is sufficiently supported by available evidence, a multimodal prognostication approach is recommended in all patients.

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1. Introduction

Severe neurological impairment caused by hypoxic-ischaemic brain injury is common after resuscitation from cardiac arrest.¹ Early identification of patients with no chance of a good neurological recovery will help to avoid inappropriate treatment and provide information for relatives.

In 2006² a landmark review from the Quality Standards Subcommittee of the American Academy of Neurology (AAN) recommended a sequential algorithm to predict poor neurological outcome in comatose survivors within the first 72 h after cardiopulmonary resuscitation (CPR). According to that algorithm, the presence of myoclonus status epilepticus on day 1, the bilateral absence of the N20 wave of somatosensory evoked potentials (SSEPs) or a blood concentration of neuron specific enolase (NSE) above 33 mcg L^{-1} at days 1–3, and absent pupillary and corneal reflexes or a motor response no better than extension (M1–2) at day 3 accurately predicted poor outcome. However, the AAN recommendations need updating:

1. The AAN 2006 review was based on studies conducted before the advent of therapeutic hypothermia (TH) for post-resuscitation

[☆] This manuscript has been endorsed by the European Resuscitation Council (ERC) and the European Society of Intensive Care Medicine (ESICM). This article is being simultaneously published in Resuscitation and Intensive Care Medicine [ISSN: 0342-4642 (print version) ISSN: 1432-1238 (electronic version)].

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Maine Medical Center
Neuroscience Institute

Case presentation (1)



- 65 yo man collapsed at baseball game
 - 26 minutes CPR, VF, defibrillation x 4, epinephrine x 3mg, intubated in field

Good Outcome!

- Continuous, slow EEG background, occasional PEDs
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Case presentation (2)



- 65 yo man collapsed at baseball game
 - 26 minutes CPR, VF, defibrillation x 4, epinephrine x 3mg, intubated in field

Bad Outcome!

- Flat EEG background, occasional PEDs
- About 11 hours into TTM at 33C, facial twitch, then generalized jerking movements