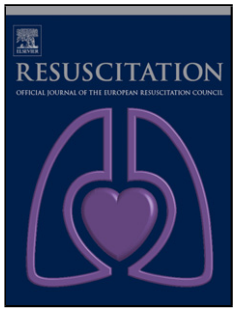

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Electro-clinical Characteristics and Prognostic Significance of Post Anoxic Myoclonus

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Abstract:

Objective: To systematically examine the electro-clinical characteristics of post anoxic myoclonus (PAM) and their prognostic implications in comatose cardiac arrest (CA) survivors.

Methods: Fifty-nine CA survivors who developed myoclonus within 72 hours of arrest and underwent continuous EEG monitoring were included in the study. Retrospective chart review was performed for all relevant clinical variables including time of PAM onset ("early onset" when within 24 hours) and semiology (multi-focal, facial/ocular, whole body and limbs only). EEG findings including background, reactivity, epileptiform patterns and EEG correlate to myoclonus were reviewed at 6, 12, 24, 48 and 72 hours after the return of spontaneous circulation (ROSC). Outcome was categorized as either with recovery of consciousness (Cerebral Performance Category (CPC) 1-3) or without recovery of consciousness (CPC 4-5) at the time of discharge.

Results: Seven patients (11.7%) regained consciousness, including 6/7 (85.7%) of the patients with early onset PAM. Patients with recovery of consciousness had shorter time to ROSC, and were more likely to have preserved brainstem reflexes and normal voltage background at all times. No patient with suppression burst or low voltage background (N=52) at any point regained consciousness. In the subset where precise electro-clinical correlation was possible, all (5/5) those with recovery of consciousness had multi-focal myoclonus and most (4/5) had midline-maximal spikes over a continuous background. No patient with any other semiology (N=21) regained consciousness.

Conclusions: Early onset PAM is not always associated with lack of recovery of consciousness. EEG can help discriminate between patients who may or may not regain consciousness by the time of hospital discharge.

Introduction

Acute post anoxic myoclonus (PAM) is seen in 16-20 % of cardiac arrest (CA) survivors [1-3]. However, accurate estimation of its true prevalence is challenged by heterogeneous definitions and variability in time of assessment across studies. The terms post-anoxic myoclonus, status myoclonus, and myoclonic status epilepticus have all been used interchangeably [2, 4-6] without a uniform description. Despite the limitations of heterogeneous definitions and descriptions of PAM, seminal work in this area has led to the perception, espoused in 2006 American Academy of Neurology guidelines, that PAM is pathognomonic for poor outcome, mainly death [6, 7]. This dogma, limited by the self-fulfilling prophecy bias of early withdrawal of life sustaining therapy (WLST), is being challenged by emerging data demonstrating functional recovery in some of these patients [8-10] and the identification of factors associated with better outcomes, such as lack of background attenuation, presence of reactivity and absence of concurrent epileptiform discharges [3, 8, 9]. These emerging studies have led to reconsideration of myoclonus itself as a poor prognostic marker in the updated 2014 European Society of Intensive Care Medicine (ESICM) guidelines [10]. To our knowledge, only one study has demonstrated two distinct EEG patterns associated with contrasting clinical courses in patients with PAM [2] .

Despite reports of functional recovery in a subset of patients, PAM remains a marker of poor outcome overall. Therefore, it is of paramount importance to identify early predictors of recovery of consciousness, which, in practice, may translate into tailoring the timing of definitive prognostication in a subset of CA survivors. This could prevent inappropriate early WLST in those with favorable prognosis, as well as futile continuation of therapy in those destined for poor outcome. The objective of this study was to systematically examine the electro-clinical characteristics of PAM and their prognostic implications. We hypothesized that the functional

outcome associated with PAM is variable and that certain EEG signatures, such as background continuity and preserved reactivity, are more predictive of recovery of consciousness.

Methods

Study Cohort

We performed a retrospective chart review on consecutive adult (≥ 18 years) CA survivors, including respiratory arrest with ensuing CA as well as primary CA, occurring in- and out of hospital, admitted to a single tertiary care center between January 2011 and November 2016. Patients were admitted to either medical, surgical, cardiac or neuro- intensive care units. Patients with PAM within 72 hours of CA were identified by chart review from clinical notes and EEG reports. We included patients regardless of whether they received targeted temperature management (TTM). Patients with continuous EEG (cEEG) monitoring lasting < 24 hours in the first 72 hours or those transferred from outside facility > 48 hours after CA were excluded from the analysis. The Yale Institutional Review Board approved this study and granted waiver of consent due to its observational nature. Twenty-five patients in this cohort were also included in a previously published study from our institution [9].

Standard Post-Cardiac Arrest Care

According to our institutional protocol, all resuscitated patients (regardless of initial rhythm) who did not regain consciousness after return of spontaneous circulation (ROSC) underwent consideration for TTM treatment. TTM to a goal of 33 or 36 degrees Celsius (^{0}C)was initiated early (always within 6 hours of CA), maintained for 24 hours with an external cooling device, the Arctic Sun®, followed by controlled rewarming. All patients were monitored on cEEG for at least 72 hours unless they regained consciousness, died or underwent WLST. Monitoring was

initiated as early as possible and usually commenced within 6-12 hours of CA. All patients received sedation and analgesia with continuous or intermittent infusions of propofol or benzodiazepines, occasionally combined with fentanyl, with dosing adjustments as clinically indicated. Neuromuscular blockade was used continuously or intermittently if shivering was refractory to other measures. Patients were evaluated and examined by the neurology team at least twice during the admission (first during or prior to cooling and later after rewarming and weaning of sedation). EEGs were read and reported at least twice daily by a critical care EEG team staffed by a board certified epileptologist with experience in critical care EEG monitoring. No primary seizure prophylaxis was used. Treatment of seizures and PAM with anti-seizure medications ± anesthetic infusions were at the recommendation of the treating neurologists. Neuroprognostic assessments occurred generally at or later than 72 hours post-CA, and included features of the clinical examination (pupillary and corneal reflexes), cEEG findings, other ancillary tests (computed tomography (CT) and/or brain magnetic resonance imaging (MRI), as well as median nerve somatosensory evoked potentials (SSEP)) in selected number of cases. Utilization of all the ancillary tests, including cEEG for neuroprognostication, was at the discretion of the treating neurologist.

Clinical Variables

The following clinical variables were collected: age, gender, time to ROSC, time to start of cEEG, CA rhythm (ventricular fibrillation/ventricular tachycardia vs. asystole or pulseless electrical activity (PEA)), type of arrest (primary cardiac, respiratory followed by cardiac, or undetermined), TTM treatment, analgesia/sedation details, neuromuscular blockade, anti-seizure medications, brainstem reflexes and best motor examination within initial 24 hours and at 48-72

hours from CA, time of onset and the characteristics of PAM. The semiology of myoclonus was ascertained initially from review of the videos (39/59), followed by review of the detailed clinical notes and EEG reports to assess for concordance. Myoclonus was classified according to area of the body involved: facial/ocular (predominantly involving jaw, eyelids (including tonic eye opening) and forehead), whole body (predominantly axial or synchronous involvement of axial and appendicular musculature, trunk and face), multifocal (asynchronous involvement of > 2 body parts), and limbs only (involvement of unilateral or bilateral extremities only).

Outcomes

The primary outcome of the study was recovery of consciousness with ability to follow commands, corresponding to a Cerebral Performance Category (CPC) score of 1-3 at the time of discharge. Outcome was scored by two board-certified neurologists (C.B.M. and A.S.) who were blinded to details of the case by reviewing the assessments from the rehabilitation team and physician's documentation. For non-survivors, the cause of death or underlying reason behind decisions of WLST was classified as medical, neurologic, cardiac (i.e., re-arrest) or brain death after careful review of documentation pertaining to goals-of-care decision-making. Secondary outcomes included time to regaining consciousness, functional outcome at last available follow up and time to WLST.

EEG Acquisition and Classification:

EEG was acquired using 21 electrode contacts, the 10-20 international system of electrode placement and one of several standard clinical digital video EEG systems. Two board-certified neurologists (M.B.D. and E.J.G.), including 1 board certified neurophysiologist (E.J.G.), who were blinded to outcomes reviewed the video EEG. Five minute EEG clips at 6, 12, 24, 48 and

72 hours after ROSC were reviewed for the following characteristics: background continuity, reactivity, and presence of epileptiform patterns (periodic discharges (PDs), lateralized rhythmic delta activity (LRDA), spike and wave (SW), sporadic epileptiform discharges (sED))[9]. Available video (39/59) was used for precise electro-clinical correlation of myoclonus. Background characteristics and epileptiform patterns were classified using the American Clinical Neurophysiology Society (ACNS) standardized critical care EEG terminology [12] (Supplemental Table 1) and (Figure 1). All recordings with suppression burst (SB) within the first 24 hours were further analyzed to assess for identical bursts defined as consecutive bursts with visually identical morphology [13]. Reactivity was assessed at least once daily and defined as any reproducible change in the background (either amplitude or frequency) with sequential incremental level of stimulation i.e., auditory (calling the patients name quietly, then loudly), followed by gentle tactile stimulation and finally with noxious stimulation (trapezius squeeze, nasal tickle and nailbed pressure). Reactivity was categorized as reactive, nonreactive, or "SIRPIDs-only" for those in whom the only reactivity was stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) [14].

Statistical Analysis:

Statistical analysis was performed using IBM SPSS Statistics v 20.0 (IBM Corp., Armonk, NY). Data were analyzed using Fisher's exact test for categorical variables and Mann-Whitney U test for continuous variables. A two-sided p value <0.05 was considered statistically significant. Due to some missing data, the denominator indicated the number of patients analyzed for each variable.

Results

Clinical Characteristics

Two hundred and eighty consecutive CA survivors were identified during the study period, of whom 62 (22.1%) developed PAM. Three of the 62 patients were excluded due to lack of EEG data within the first 72 hours, resulting in final cohort of 59 patients. Survival to hospital discharge occurred in 10/59 patients (16.9%), of whom 7/59 (11.9%) regained consciousness. We further compared patients who regained consciousness (CPC 1-3) with patients in persistent vegetative state or dead (CPC 4-5) (Table 1). Patients with recovery of consciousness had shorter time to ROSC (median [IQR], 6 [3.5 – 12.5] vs. 18 [10 – 23.5] minutes; p=0.011) as well as more preservation of brainstem reflexes at 48-72 hours (pupillary reflex (100% vs. 41.3%, p=0.004), corneal reflex (85.7% vs. 28.3%, p=0.006), and gag reflex (100% vs. 28.9%, p=0.001)) and flexor or better motor response (71.5% vs. 11.8 %; p= 0.002). Myoclonus occurred early (< 24 hours post-CA) in most patients, with no difference between patients who regained consciousness and patients who did not (6/7, 85.7% versus 45/52, 86.5%, p=1.000). There was no difference in age, sex, type of arrest, arrest rhythm, the use of TTM, sedation, use of paralytic, or number of anti-seizure medications utilized between the two groups. The most common anti-seizure medications used were levetiracetam (43/59, 72.9%) followed by valproic acid (20/59, 33.9%), phenytoin (9/59, 15.3%), and others (clobazam, lacosamide and clonazepam) (9/59, 15.3%).

Background EEG Patterns and Evolution

Patients who regained consciousness had normal voltage background (7/7, 100%) at all time points, whereas no patient with a poor outcome had normal voltages at all examined time points within 72 hours (0/52) (Figure 2 and 3). In patients without recovery of consciousness, the most common background finding in the first 24 hours was SB (59.3% at 6 hours, 78.6% at 12 hours,

and 65.3% at 24 hours) (Figure 3B). In the 42 patients who had SB in the first 24 hours, the majority (38/42, 90.5%) had identical bursts. There was no difference in the prevalence of discrete electrographic seizures between the two groups (1/7, 14.3% vs. 11/52, 21.2%, p=0.562) or epileptiform patterns (5/7, 71.4 % vs. 25/52, 48.1%, p=0.424) (Figure 2). There was no difference in the EEG background, reactivity and epileptiform patterns between the patients who received TTM at 33 ^{0}C, 36 ^{0}C or no TTM (Supplemental Table 2).

EEG Reactivity

Preserved EEG reactivity was more common in patients who regained consciousness (4/7, 57.1 % vs. 5/52, 9.6%, p=0.006). In those with preserved reactivity, 4/9 (44.4%) regained consciousness. In patients without reactivity, only 2/47 (4.3%) patients regained consciousness. Among patients with SIRPIDs-only 1/3 (33.3%) had recovery of consciousness.

Electro-clinical Characteristics of Myoclonus

Of all the patients, 39/59 (66.1%) had video recordings available for precise electro-clinical correlation (Table 2). Only patients with multi-focal myoclonus regained consciousness whereas no patient with any other semiology had recovery of consciousness (5/18 with multifocal myoclonus vs 0/21 with other semiology, p=0.015). In these patients, myoclonus was associated with frequent, sporadic, low amplitude midline-maximal spikes over a continuous background (Figure 1B) in 4/5 (80%) and generalized spike wave discharges (GSW) with normal voltage background in 1/5 (20%). In patients without recovery of consciousness, myoclonus time-locked to highly epileptiform bursts in SB pattern was seen in 24/34 (70.6%) patients (Figure 1A), while blunt cortical bursts were seen in 5/34 (17.6%) patients (Figure 1C). In 4 of 34 patients (11.8%),

myoclonus was not associated with any cortical activity and occurred during the suppressed portions of EEG background, creating a myogenic artifact (Figure 1D). None of these 4 patients regained consciousness.

In the remainder of patients (20/59), myoclonus had either resolved spontaneously without any treatment prior to cEEG (1/7, 14.3% vs 4/52, 7.7%), or resolved after administration of paralytic and did not recur later while on cEEG (1/7, 14.3% vs 6/52, 11.5%), or the myoclonus was recorded on cEEG however video was later deleted during the archiving process (7/52, 13.5%, all in the group who did not regain consciousness).

Ancillary tests

Among patients with early normal CT, 6/40 (15%) regained consciousness. There was no difference in the percentage of patients with early normal CT between the two groups (6/7, 85.7% vs 34/50, 68%, p=0.662). In those with normal MRI, 4/5 (80%) had recovery of consciousness. Those with normal MRI were significantly higher in the patients who regained consciousness compared to those who did not (4/6, 66.7% vs 1/26, 3.8%, p=0.002). SSEPs were only performed in 15 patients, none of whom regained consciousness and for the majority of whom the N20 responses were absent (13/15, 86.7%)

Outcomes and WLST

At the time of discharge, 10/59 patients survived, of whom 3 had a CPC score of 4, and 7 had a CPC score of 3. In the patients who recovered consciousness, the median time to recovery of consciousness was 11 days (IQR, 6 – 14). Among nonsurvivors (49), deaths related to WLST were 81.6% (40/49); perceived poor neurologic prognosis drove WSLT in most patients (37/49,

75.5%) rather than perceived poor medical prognosis (3/49, 6.1%). Eight out of 49 patients (16.3%) were declared brain dead and 1 re-arrested. The median time to WLST (40/49) was 5 days (IQR 4- 12.7), which was significantly shorter compared to the time to regaining consciousness among survivors (11 days; $p < 0.001$).

Of survivors in a persistent vegetative state (3), 2 died within 3 months and 1 died within 12 months of CA. Among the 7 survivors with a CPC of 3, the last available follow up ranged from 20- 48 months during which 2 patients became independent, 1 patient re-arrested at 20 months and the remainder (N=4) continued to require assistance with feeding or ambulating (CPC 3).

Discussion

In our cohort, PAM occurred in 59 (22.1%) CA survivors; 7/59 (11.9%) regained consciousness, including 6/51 (11.8%) with early-onset myoclonus (within the first 24h). Patients who regained consciousness had multi-focal myoclonus (5/5), and EEG demonstrated frequent sporadic midline-maximal spikes on a continuous background (4/5), consistent with 1 prior study [2]. EEG features of normal voltage background during the first 72 hours of CA and preserved brainstem reflexes at 48-72 hours were associated with recovery of consciousness regardless of the presence of epileptiform EEG patterns (7/7). Our study suggests that early PAM is not uniformly associated with lack of recovery of consciousness and that EEG is helpful in discriminating between patients who may or may not regain consciousness.

In our study, the primary outcome measure was recovery of consciousness (CPC 1-3) as opposed to complete independence (CPC 1-2) at the time of hospital discharge, as seen in multiple prior studies. Historically, PAM was associated with a universally dismal outcome,

particularly from WLST due to perceived poor neurologic recovery, limiting our understanding of the natural history of patients who may show recovery of consciousness, but do not progress to independence (CPC 3) at hospital discharge. In a large multicenter study of PAM, WLST occurred in 330 of 427 patients, of which 89% were due to neurological futility [3]. In this study, median time to WLST was 5 days as opposed to the length of hospital stay of 14.5 days in those with good outcome. Since our current outcome assessment scales lack granularity, there is also incongruity about the clinical significance of CPC 3 in the scientific community [15], which may be resolved by using an extended approach with more functional domains, such as cerebral performance category –extended (CPC-E) [16]. In our cohort, the median time to WLST (5 days) was significantly shorter than time to regaining consciousness (11 days). This delayed recovery of consciousness may have been due to aggressive treatment with anesthetics and residual effects of sedation. Additionally, functional recovery changes over time in CA survivors [17, 18]. Due to these varied factors as well as complications related to prolonged ICU stays, all of which impact recovery, categorizing CPC 3 as a favorable outcome at hospital discharge is reasonable and consistent with studies reporting outcomes in similar cohorts [4, 8, 19].

Results from our study are in accordance with prior studies in which cEEG background was a robust and reliable predictor of outcome in comatose CA survivors as early as 12- 24 hours [9, 20-24]. In our study, no patient with recovery of consciousness had SB at any time point, which contrasts with some studies reporting favorable outcomes even in patients with SB [1, 20, 25]. These studies utilized either propofol or the details of anesthetics used were not clearly outlined; whereas midazolam was used in most of our patients. Additionally, many patients in our cohort had identical bursts, a variant of SB which has been associated with fatal outcome

[13]. These findings suggest that SB in our cohort may be a marker of severity of neuronal injury rather than a drug-induced pattern, and hence poor outcome.

Literature on semiology of PAM is scarce and is limited by heterogeneity in terminology across studies. Myoclonus of cortical origin is described as asynchronous, multi-focal, predominantly involving distal musculature; EEG spikes time locked to the electromyography (EMG) bursts and often associated with giant cortical SSEP response [26, 27]. In contrast, brainstem (reticular) myoclonus preferentially involves axial and proximal musculature, not time locked to EEG bursts and EMG demonstrates sequential recruitment pattern of muscles innervated by the brainstem nuclei on EMG [27, 28]. Although detailed neurophysiological testing was not performed in our patients, multi-focal semiology in those who regained consciousness, of which 4/5 patients demonstrated midline-maximal low amplitude spikes, on a continuous EEG background, suggests cortical origin. No patient with any other semiology regained consciousness. A peculiar form of myoclonus with eyelid opening is often associated with bursts of SB [29, 30]. None of the 9 patients with this finding regained consciousness in our cohort. The generator of this phenomenon has been debated in the literature and further studies are required to understand this mechanism. Studies examining the semiology in PAM with a standardized classification in relation to prognostic implications are required.

Our findings are consistent with a recent study in which a continuous background with midline-maximal spikes time-locked with myoclonus was associated with favorable outcome, whereas a SB background indicated poor outcome [2]. This pattern of midline-maximal spikes on a continuous background is akin to EEG findings described in Lance-Adams syndrome (LAS) [31]. LAS is a sub-acute to chronic form of PAM that usually develops a few days after resolution of coma [32], although there are reports where the first sign of myoclonus developed

during comatose state [31]. Therefore, it has been postulated that patients regaining consciousness after PAM in the TTM era may represent an early form of LAS, with awakening being masked by sedatives [2, 25, 33, 34]. While this is certainly a possibility, it should be noted that the largest case series of LAS included only 14 patients [35]. Future systematic prospective studies examining the onset, semiology, and possibly more refined electrophysiologic analysis using EEG, EMG and back averaging techniques for comparing PAM and LAS are required to elucidate the various subtypes of myoclonus and their impact on outcome as further validation of these hypotheses.

Our study was limited by small number of subjects, its retrospective nature and lack of outcome data at 3 and 6 months. The clinical teams had access to the cEEG findings, which may have influenced the decision-making process including WLST, introducing the self-fulfilling prophecy bias inherent to all CA studies to date. Factors such as frequency and duration of myoclonus, its response to treatment and how that impacted the decision for WLST was not discernable due to the retrospective nature of the study. Most of the patients were treated with ≥ 2 anti-seizure medications ± anesthetic infusions, which suggests that a fair therapeutic trial was pursued; however, this remains speculative as limited data were obtained on the exact doses of medications. The occasional use of neuromuscular blockade limited accurate characterization of the clinical semiology and precise electro-clinical correlation of myoclonus in the entire cohort, a challenge commonly encountered in studies in this setting. Ancillary tests such as MRI, and median nerve SSEPs were not performed in all patients and hence their prognostic value in this cohort could not be determined. Despite these limitations, ours is the one of the few studies, which provides precise and nuanced electro-clinical correlation for PAM and its prognostic significance. Future studies illuminating the details in semiology, duration and EEG

characteristics of PAM are needed. Universal criteria for defining and classifying PAM and myoclonic status epilepticus would allow for a more meaningful comparison amongst studies. Moreover, further prospective studies in a setting where the practice of WLST is uncommon are required to understand the short and long-term implications on outcome.

Conclusions

In summary, our study demonstrated that despite early onset PAM, some patients do regain consciousness and regain independence. Continuous background ± multi-focal myoclonus, time-locked midline-maximal spikes in the first 72 hours after CA along with preserved brainstem reflexes are likely strong predictors of recovery of consciousness in patients with PAM. Future multicenter studies are necessary to validate these findings.

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Figure captions

Figure 1: Representative EEG recordings for background classification.

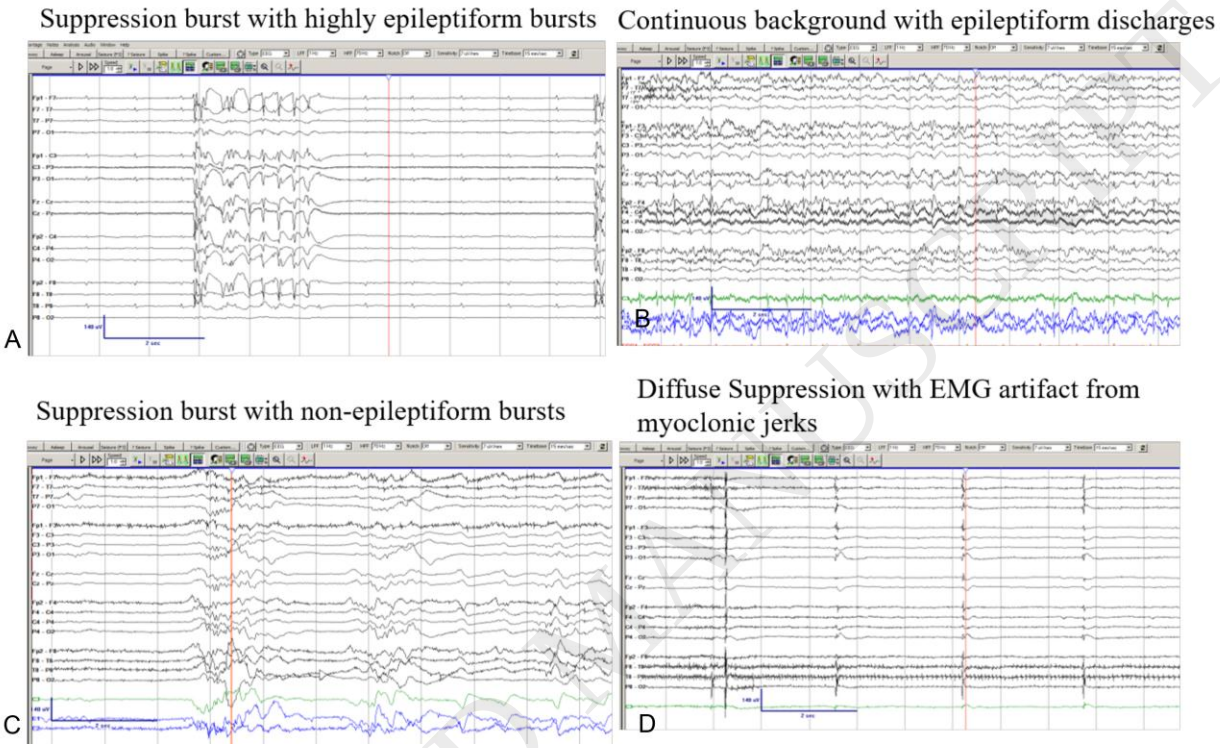

Figure 2: Comparison of EEG characteristics in patients with recovery of consciousness and those without recovery of consciousness

[a] Included periodic discharges, lateralized rhythmic delta activity and sporadic epileptiform discharges,

*p <0.05

NV, normal voltage

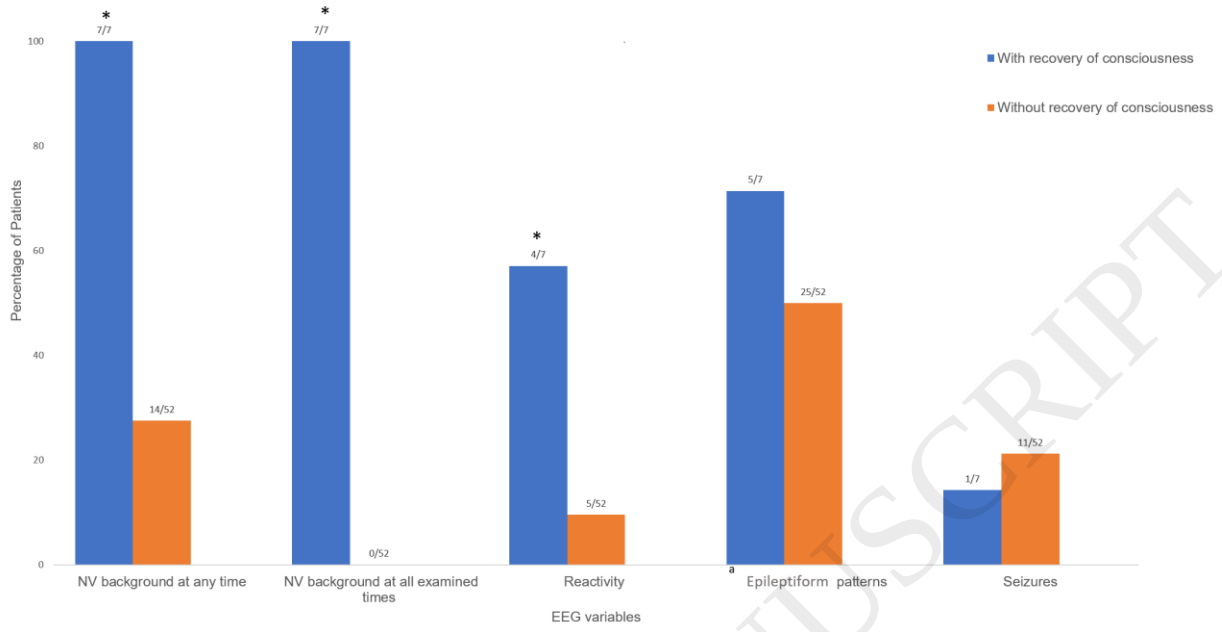

Figure 3: Evolution of EEG patterns in patients with recovery of consciousness (3A) and those without recovery of consciousness (3B). The number at the top of each bar indicates the number of patients examined at each time point.

NV, normal voltage; ED, epileptiform EEG patterns (Included periodic discharges, lateralized rhythmic delta activity and sporadic epileptiform discharges,); SB, suppression burst, SUP/ATT, suppressed/attenuated; ROSC, return of spontaneous circulation

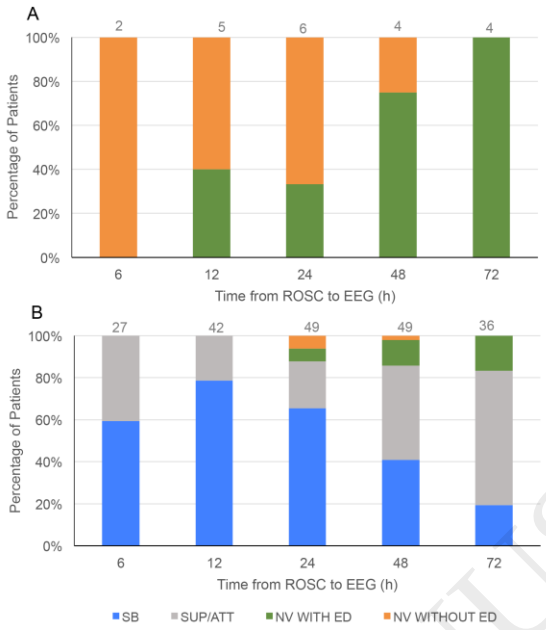

Table 1: Clinical characteristics of the study population

Characteristics	Patients with regained consciousness (N=7)	Patient without recovery of consciousness (N= 52)	P value
Age (years)	52 (45-70)	58 (45- 66)	0.991
Sex (Male)	4/7 (57.1%)	29/52 (55.8%)	1.000
Time to ROSC (min)	6 (3.5-12.5)	18 (10-23.5)	0.011*
Time to start of EEG (hours)	12 (6-26)	8 (6-12)	0.256
Arrest cardiac rhythm			0.615
VF/VT	2/6 (33.3%)	11/50 (22.0%)	
PEA/Asystole	4/6 (66.7)	39/50 (78.0%)	
Type of Arrest			0.221
Cardiac	4/7 (57.1%)	14/52 (26.9%)	
Respiratory	3/7 (42.9%)	32/52 (61.5%)	
Undetermined	0/7 (0%)	6/52 (11.5%)	
Targeted temperature management (TTM)	4/7 (57.1%)	40/52 (76.9%)	0.340
Initial (<24 h) Brainstem Reflexes Present			
Pupillary Reflex	5/7 (71.4%)	19/52 (36.5%)	0.109
Corneal Reflex	4/6 (66.7%)	8/44 (15.4%)	0.014*
Gag or cough reflex	4/7 (57.1%)	12/50 (24.50%)	0.088
Oculocephalic reflex	3/6 (50%)	4/42 (9.5%)	0.033*
All reflexes Absent at 24 h	1/7 (14.3%)	31/52 (59.6%)	0.040*
Repeat (48-72 h) Brainstem Reflexes Present			
Pupillary Reflex	7/7 (100%)	19/46 (41.3%)	0.004*
Corneal Reflex	6/7 (85.7%)	13/46 (28.3%)	0.006*
Gag or cough reflex	7/7 (100%)	13/45 (28.9%)	0.001*
Oculocephalic reflex	3/5 (60%)	9/40 (22.5%)	0.109
All reflexes Absent	0/7 (0%)	22/45 (48.9%)	0.016*
Best Motor Response			
Flexor or better	5/7 (71.4%)	6/52 (11.5%)	0.002*
Sedation			0.279
Midazolam	5/7 (71.4%)	24/52 (46.2%)	
Propofol	0/7 (0%)	13/52 (25.0%)	
Midazolam and Propofol	2/7 (28.6%)	15/52 (28.8%)	
Paralytic	3/7 (42.9%)	29/52 (55.8%)	0.692
Anti-epileptic medication			0.455
1	1/7 (14.3%)	20/52 (38.5%)	

≥2	4/7 (57.1%)	21/52 (40.4%)	
None	2/7 (28.6%)	11/52 (21.2%)	
Time of Onset of Myoclonus			1.000
< 24 hours	6/7 (85.7%)	45/52 (86.5%)	
24-72 hours	1/7 (14.3%)	7/52 (13.5%)	
Normal Imaging			
CT	6/7 (85.7%)	34/50 (68%)	0.662
MRI	4/6 (66.7%)	1/26 (3.8%)	0.002

ROSC, return of spontaneous circulation; EEG, electroencephalography, VF, ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity, CT, computed tomography; MRI, magnetic resonance imaging

Table 2: Clinical and electrographic features of myoclonus in the subset of patients with precise electro-clinical correlation (N= 39)

Variables	Patients with recovery of consciousness (N=5)	Patient without recovery of consciousness (N=34)	P value
Time of onset of myoclonus			0.436
< 24 hour	4/5 (80%)	31/34 (91%)	
24- 72 hours	1/5 (20%)	3/34 (8.8%)	
Semiology			0.082
Facial/Ocular	0/5 (0%)	9/34 (26.5%)	
Whole body	0/5 (0%)	10/34 (29.4%)	
Limbs only	0/5 (0%)	2/34 (5.9%)	
Multi-focal*	5/5 (100%)	13/34 (38.2%)	**0.015
Underlying EEG correlate of myoclonus			<0.001
Highly epileptiform bursts	0/5 (0%)	24/34 (70.6%)	
Blunt cortical bursts	0/5 (0%)	6/34 (17.6%)	
Midline-maximal spikes	4/5 (80%)	0/34 (0%)	
GSW discharges	1/5 (20%)	0/34 (0%)	
No cerebral correlate	0/5 (0%)	4/34 (11.8%)	

**, p value comparing multi-focal myoclonus to all other semiologies (facial/ocular, whole body and limbs only).

EEG, electroencephalography; SB, suppression burst; GSW, generalized spike and wave