Title: Characteristics and role in outcome prediction of continuous EEG after status epilepticus: A prospective observational cohort.
Authors: Alvarez V, Drislane FW, Westover MB, Dworetzky BA, Lee JW
Journal: Epilepsia
Year: 2015 Jun
Volume: 56
Issue: 6
Pages: 933-41
DOI: 10.1111/epi.12996

Characteristics and Role in Outcome Prediction of continuous EEG after Status Epilepticus: a prospective observational cohort

Running title: cEEG and outcome prediction after SE

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Content:

Title: 125 characters including spaces; Abstract: 250 words; Body of Manuscript: 3287 words
4 tables; 0 figures, 35 references

Search Terms:

Neurocritical care – Terminology – Status epilepticus – EEG background activity

Abstract:

Objective: Continuous electroencephalography (cEEG) is important for treatment guidance in status epilepticus (SE) management, but its role in clinical outcome prediction is unclear. Our aim is to determine which cEEG features give independent outcome information after correction for clinical predictor.

Methods: cEEG data of 120 consecutive adults patients with SE were prospectively collected in three academic medical centers using the 2012 American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology. Association between cEEG features and two clinical outcome measures (mortality and complete recovery) was assessed.

Results: In the first 24 hours of EEG recording, 49 patients (40.8%) showed no periodic or rhythmic pattern, 45 (37.5%) had periodic discharges, 20 (16.7%) had rhythmic delta activity, and 6 (5%) had spike-and-wave discharges. Seizures were recorded in 68.3% of patients. After adjusting for known clinical predictive factors for mortality including the Status Epilepticus Severity Score (STESS) and the presence of a potentially fatal etiology, the only EEG features (among rhythmic and periodic patterns, seizures, and background activity), that remained significantly associated with outcome were the absence of a posterior dominant rhythm (OR: 9.8; $p = 0.033$) for mortality and changes in stage II sleep pattern characteristics (OR: 2.59 for each step up among these categories: absent, present and abnormal, normal; $p = 0.002$) for complete recovery.

Significance: After adjustment for relevant clinical findings, including SE severity and etiology, cEEG background information (posterior dominant rhythm and sleep patterns) is more predictive for clinical outcome after SE than are rhythmic and periodic patterns or seizures.

Key words:

Neurocritical care – Terminology – Status epilepticus – EEG background activity

Introduction:

Status epilepticus (SE) is a potentially fatal condition requiring comprehensive assessment and rapid treatment [1]. Continuous electroencephalography (cEEG) has an important role in this setting for seizure detection and treatment guidance [2] and is recommended for SE management [3]. The role of continuous or repeated routine electroencephalography (EEG) in outcome prediction is less clearly defined [4], and with inconsistent findings [5], [6]. Moreover, most available data regarding EEG patterns and clinical outcome association were published before the introduction of the 2012 American Clinical Neurophysiology Society's (ACNS) Standardized Critical Care EEG Terminology [7]. This terminology clearly defines seizures, rhythmic and periodic patterns (RPP), and EEG background features. Recently a high inter-rater agreement has been reported using this terminology [8]. Although recent studies have examined some EEG pattern and seizures using this terminology [9], the relationship between EEG patterns categorized by this terminology and SE outcome has not been evaluated. Here, we describe EEG patterns recorded during the first 24 hours of cEEG in a prospectively collected cohort of adult patients with SE and their association with outcome.

Methods:

- **Primary research question:**

  The primary research question was to evaluate cEEG yield in outcome prediction after SE.

- **Standard Protocol Approvals, Registrations, and Patient Consents:**

  The Institutional Review Boards of each center approved this study. As this observational study involved no risk for patients and focused on acute phase of critically ill patients, consent was waived.

- **Cohort and SE definition:**

  This observational cohort included all consecutive adult patients (> 16 years of age) with SE of all etiologies (with the exception of post-anoxic SE) admitted to three university tertiary care centers in Boston, USA, from June 1st 2013 at the Brigham and

Women's Hospital and the Massachusetts General Hospital; and from November 1st 2013 at the Beth Israel Deaconess Medical Center, all through March 31, 2014. Subjects were screened through daily review of all EEGs ordered during that period; all patients with suspected SE at each institution had continuous EEG within 24 hours as part of routine clinical care. SE was defined as the occurrence of an ongoing epileptic seizure or repeated epileptic seizures, without full recovery between seizures for more than 5 min [1]. EEG diagnosis was required for nonconvulsive SE in accordance with recently published criteria [10].

- **Definition of variables**

  The STatus Epilepticus Severity Score (STESS) was calculated for each patient using age (< 65 years = 0 pt; ≥ 65 years = 2 pts), seizure type (simple-partial, complex-partial, absence and myoclonic in the context of idiopathic/genetic epilepsy = 0 pt; generalized-convulsive = 1 pt; non-convulsive SE in coma = 2 pts), level of consciousness (alert, somnolent or confused = 0 pt; stuporous or comatose = 1 pt), and history of previous seizures (yes = 0 pt; no = 1 pt), with a total score between 0 and 6 points [11]. This score is a tool designed to predict mortality and has been externally validated on an independent cohort [12]. The onset time of SE was determined as precisely as possible from pre-hospital chart and emergency department summaries. The time last seen well was considered the beginning of SE for episodes without clear times of onset (e.g. unwitnessed or subtle nonconvulsive SE). Etiology was determined based on clinical chart review and classified as potentially fatal if not specifically treated (or not) as previously described in others studies [13], [14] including : acute (<7 days) large vessel ischemic stroke, acute cerebral hemorrhage, acute central nervous system infection, severe systemic infection, malignant brain tumor, AIDS with CNS complications, chronic renal insufficiency requiring dialysis, systemic vasculitis, metabolic disturbance or acute intoxication sufficient to cause coma in the absence of SE, eclampsia, and intracranial tumor surgery.

The presence or absence of structural brain lesions was assessed using available imaging information and categorized as: no lesion, or remote or acute structural lesion. Clinical outcome at hospital discharge was categorized as: return to pre-morbid clinical state, new morbidity, or death.

- **cEEG recordings and data classification**

Recordings were acquired using the international 10-20 system with 21 electrodes (XLTEK, Natus Medical Incorporated, San Carlos, CA). Filters were set at 0.5 and 70 Hz and a notch filter was used as needed. All EEG recordings were reviewed by trained electroencephalographers using the 2012 ACNS Critical Care EEG terminology. One author certified for ACNS Standardized Critical Care EEG Terminology (V.A.) prospectively reviewed all EEG tracings to assure accurate classification. Missing information was obtained during this secondary review. For the rhythmic and periodic patterns (RPP), "Main term 1" (lateralized, generalized, multifocal, bilateral independent) and "Main term 2" (periodic discharges (PD), rhythmic delta activity (RDA), spike-and-wave (SW), or no periodic pattern) were recorded. Modifiers regarding their prevalence, duration, frequency, and sharpness were recorded as ordered categorical variables. The "plus modifiers" were also collected when applicable [7]. For background activity, data regarding symmetry, frequency, and continuity were collected as ordered categorical variables. The posterior dominant rhythm and its reactivity were collected as categorical variables: present or absent. The presence of stage II sleep was also recorded as ordered categorical variables (absent, present but abnormal or present and normal). Stage II sleep pattern were considered as normal if K-complexes and spindles were present, symmetric and synchronous; otherwise it was considered as present and abnormal or absent. Presence of definite seizures and their frequency (number of seizures / hours) were also assessed. Each

patient was categorized as to the presence of electrographic-only seizures or not. For nonconvulsive seizures, the Young criteria were used [15].

- **Statistical analysis**

  Data were analyzed using Stata 13 (StataCorp, College Station, Texas, USA). Patients with different types of RPP were compared using χ^2, Fisher's exact, and Kruskal-Wallis tests, as appropriate. Univariate analyses for clinical measures, etiology, and cEEG features (RPP, seizures and background) were conducted for the two outcomes of interest (mortality and complete clinical recovery). Variables with a p-value ≤ 0.05 were entered into a stepwise backward logistic regression model (significance level for removal from the model: $p < 0.05$). Model goodness-of-fit was evaluated with the Hosmer-Lemeshow χ^2. Model performance was assessed through receiver operating characteristics (ROC) curve analysis.

Results:

During the study period, 120 adult patients undergoing cEEG for SE met criteria for inclusion in the study. The mean age was 58 years (SD: 16.65). Fifty-six patients were male (46.7%), 62 (51.6%) had premorbid seizures. The median STESS value was 2 (range: 0 – 6), and 50% of patients had a potentially fatal etiology.

cEEG recordings were obtained at a median time of 14.4 hours (range: 0 – 143 hours) after commencement of SE. Twenty-two SE episodes (18.3%) started while the cEEG was being acquired. **Table 1** summarizes the clinical findings for patients with different RPP types. While 49 patients (40.8%) did not show any periodic pattern, 45 (37.5%) had PD, 20 (16.7%) RDA, and 6 (5.0%) SW. The type and presence of a period pattern was differentially distributed depending on age. Patients without RPP were younger (mean, 51.0 years old) than patients with PD (61.0 years), RDA (66.3 years) or SW (63.5 years) ($p < 0.001$). Patients with SW and without RPP had a potentially fatal etiology less frequently ($p = 0.043$). Approximately half of patients without RPP and half of those with SW did not have any structural lesion whereas the

majority of PD and RDA were associated with a remote or acute structural brain lesion (p = 0.009). Of note 116/120 patients (96.7%) had brain imaging; 111 patients had a CT, 60 an MRI and 55 patients had two imaging modalities. All four patients without imaging had a SE in the setting of a known epilepsy (three with AED-related events and one without any provocative factor) and were not considered in this analysis.

Seizures were less frequent in patients without RPP, but the clinical nature of seizure type (clinical or purely electrographic) was the same across the four groups.

RPP characteristics are shown in **Table 2**. While 73.4% of PD were abundant or continuous, and SW were mostly continuous, 55% of RDA were frequent or occasional (p = 0.003). The duration of the pattern (when non-continuous) also differed, with PD being more prolonged than RDA of SW (p = 0.006). The RPP frequency was also lower in the PD group than in the RDA or SW groups (p < 0.001, Kruskal-Wallis). The descriptions of the sharpness and the "plus modifiers" are shown, but their comparisons were not performed because these terms do not apply uniformly to all RPP. Of note, only 2/45 of the PD (4.7%) had triphasic morphology.

EEG features, clinical information and etiology of survivors and non-survivors are compared in **Table 3**. RPP were more frequently absent in the survivors (43.1% vs. 33.0%), and generalized rhythmic delta activity (GRDA) was more frequent in the non-survivors (27.8% vs. 2.0%) (p = 0.002). A background with a posterior dominant rhythm (PDR) was present in nearly half of the survivors but in only 5.6% of patients who died (p = 0.001). The background frequency was also slower in the non-survivors, with more patients with delta activity and fewer patients with alpha activity than in the survivors (p = 0.01). Clear background reactivity was seen twice as often in the survivors (p = 0.018). All other EEG features regarding RPP modifiers, seizures and background (including background symmetry, voltage and continuity; not shown in Table 3) were similar between both groups.

The STESS was significantly higher in non-survivors: median of 4 (range: 1 – 6) vs. 2 (0 – 6, p = 0.0018). Non-survivors were also twice as likely to have a potentially fatal etiology (p = 0.004, Fisher). In multivariate analysis, only the absent of a PDR (OR: 9.8; 95% CI: 1.2 – 79.8;

p = 0.033) and the STESS (OR: 1.48/point; 95% CI: 1.06 – 2.05; p=0.02) remained associated with mortality (model goodness-of-fit: p = 0.72, χ^2). The area under the ROC curve using the PDR and the STESS to predict mortality was 0.79 (95% CI: 0.695 – 0.894).

Patients with full recovery at hospital discharge and those presenting new morbidity (including non-survivors) are compared in **Table 4**. Patients with good recovery had RPP less frequently (32.1% vs. 61.5%, p = 0.007) and had less frequently seizures (53.9% vs. 75.3%, p = 0.022). Nevertheless, when present, seizure types and frequency were similar in both groups. A PDR was also seen more frequently in patients with favorable outcomes. Stage II sleep patterns were present and normal in more than half of patients with complete recovery, but in only in 13.6% of patients with new morbidity or death (p < 0.001). All other EEG features regarding RPP, seizures, or background (including background symmetry, voltage, and continuity; not shown in Table 4) were similar. STESS was lower in patients with good outcome: median of 2 (range: 0 – 6) vs. 3 (0 – 6, p < 0.001). Those patients also had a potentially fatal etiology less frequently. In the multivariate logistic regression model, STESS (OR: 0.51/point; p = 0.005; 95% CI: 0.32 – 0.82) and the presence of a potentially fatal etiology (OR: 0.12; p = 0.001; 95% CI: 0.03 – 0.4) remained significant. The only EEG feature that remained significantly associated with complete clinical recovery was stage II sleep pattern characteristics (OR: 2.59/each step up: from absent to present but abnormal or from present but abnormal to normal; p = 0.002; 95% CI: 1.4 – 4.77) (model goodness-of-fit: p = 0.85, χ^2). The area under the ROC curve using the STESS, the presence of potentially fatal etiology and sleep II stage categories is 0.88 (95% CI: 0.82 – 0.94).

Discussion:

The main finding of this study is that among the cEEG characteristics considered, background activity and sleep features appear to be better clinical outcome prediction factors than RPP and seizure features -- which lost their predictive value after adjustment for other known predictors. Regression analysis including cEEG, clinical information, and etiology found that the absence of a posterior dominant rhythm was the only EEG feature associated with

mortality. When absent, it increased markedly the likelihood of mortality, with an odds ratio of 9.8. Similar findings were shown for good outcome prediction. Stage II sleep characteristics were the only significant predictor of a increased likelihood of complete recovery, with an OR of 2.59 for each step up in the following categories: absent, present and abnormal, normal. Both mortality and complete recovery models resulted in very good goodness-of-fit and prediction performance, supporting these findings.

EEG oscillations in waking state, including the posterior dominant rhythm [16] and the sleep spindles [17] are due to intact connections between the neocortex and the thalamus, also know as the thalamocortical system. Moreover a recently published study [18] suggest that EEG background organization and sleep architecture correlate with preserved cognition assessed with functional magnetic resonance imaging and brain metabolism assessed with positron emission tomography in patients with disorders of consciousness. Those finding associated with the present study suggest that the presence of a posterior dominant rhythm and sleep spindles may be clinical surrogate of the thalamocortical system integrity and confirm EEG as a valid biomarker in the epilepsy field [19].

Reports assessing the role of EEG in outcome prediction in SE are few, but some have reported similar findings. A study evaluating periodic lateralized epileptiform discharges (PLEDs) (now labeled as LPD according to the 2012 ACNS terminology) in 62 prospectively collected SE episodes also found that outcome was more closely related to age and etiology than to the ictal EEG pattern [6]. While abnormalities on EEG one hour after treatment predicted seizure recurrence in another prospective study of 70 cases of SE [20], they were not associated with mortality. In a retrospective study of the prognostic implication of different types of periodic epileptiform discharges (PDs) [21], within the same PD pattern the likelihood of death was decreased in patients with chronic etiologies (as opposed to acute etiologies) after regression analysis. Moreover, no statistical association was found between outcomes and several EEG features including RPP amplitude, inter-PD interval, and duration of epileptiform complexes.

Others have found that RPP or seizures may be useful in outcome prediction. Jaitly and colleagues found that “after SE ictal discharges” the “presence of a burst-suppression pattern” and, to a lesser extent, LPDs (formerly called PLEDs) were associated with increased morbidity and mortality after adjustment for etiology in a prospectively collected cohort of 180 patients with SE. In that study [22], however, brain anoxia represented 20% of the cohort; anoxic patients were excluded from our study. Because post-anoxic SE after cardiac arrest usually carries a dismal prognosis and is frequently associated with RPP [23], this might explain the difference in findings. Also, in that study EEG was categorized into seven different patterns and not assessed using the detailed classification used in this study [7] that allowed evaluation of each different feature of the EEG. PDs were the only EEG feature associated with outcome in a retrospective evaluation of 50 SE cases [5], with 44% of patients with PDs having a poor outcome vs. 19% in the group without PDs. Still, these results were based on a retrospective univariate analysis without adjustment for etiology or clinical findings. In our analysis, RPP were also significant predictors for both good outcome and mortality in univariate analysis, but this association was lost after adjustment for etiology and STESS. Moreover, the study by Nei and colleagues [5] focused on ictal or PDs without assessment of the EEG background. There are also divergent results regarding the value of RPP in outcome prediction in different patient populations. No association was found between PD and mortality in comatose patients [24] even when PDs were prolonged [25], but the presence of PDs was a strong outcome predictor in the setting of CNS infection [26] or intracerebral hemorrhage [27]. The fact that PDs are associated with outcome in cohorts with specific brain pathology, such as CNS infection or intracerebral hemorrhage, and not when assessing comatose patients in general or in patients with SE from all etiologies, reinforces the importance of the underlying etiology in this setting.

Among patients with RPPs, PDs were very frequent (two thirds of patients), followed by RDA and SW. Interestingly, the same rate of seizure occurrence (~ 80%) was found in the PD, RDA, and SW groups, but in only 51% when RPP were absent. The similarity of seizure occurrence in the LPD and LRDA groups has also been described in critically ill patients [9]. Indeed, both EEG patterns were associated with a rate of seizure occurrence of 60% in that

cohort. That we included patients in SE only, while and Gaspard and colleagues included unselected patients undergoing cEEG, may explain the higher rate of seizure occurrence in our cohort. Half of patients with SW and those without any RPP did not have structural brain lesions, as opposed to patients with PD or RDA, among whom 86% and 85% respectively had structural lesions. This reinforces the association of PDs with structural lesions [28] and suggests a more non-structural etiology to the spike-and-wave pattern, as seen in the genetic generalized epilepsies [29].

This study has several strengths. First, it includes data from 120 patients with SE studied prospectively using the new American Clinical Neurophysiology Society's (ACNS) Standardized Critical Care EEG Terminology [7] which has been demonstrated to be suitable for research on the clinical significance of critical care EEG features [8], as opposed to previous studies which used less uniform EEG terminology [5, 6, 20, 21, 22]. Moreover, the yield of cEEG in outcome prediction was adjusted for known important clinical factors, further confirming the robustness of the STESS for outcome prediction [11, 12].

This study has also some limitations. First, we limited our analysis to the first 24 hours of cEEG and could not exclude the possibility that later assessment or pattern evolution might have led to different findings and increased the yield of some other EEG features in outcome prediction. Nevertheless, the prognostic value of SE duration is largely lost after 10 hours [30], and early EEG evaluation has been shown to be as reliable as later assessment for outcome prediction in a different clinical setting [31]. Also, the outcome prediction value of some RPP modifiers (sharpness and “plus modifiers”) was not evaluated. Still, these particular terms cannot be applied to all RPPs, and the relatively poor inter-rater agreement reported 8 may lessen the predictive value of the “plus modifier”. Also, stepwise backward logistic regression model was employed in the present study to identify variables with independent prediction value, a technique that some consider suboptimal [32, 33]. However, a stepwise regression model in logistic regression is an efficient and widely used way to analyze the effect of a group of independent variables on a binary outcome [34, 35]. Careful variables selection was made

(know predictors, statistically significant variables in the univariate analysis) and necessary assumptions for regression [34] were checked (absence of colinearity, numbers of variable) in order to minimize the potential limitations of this procedure. Finally, this study is based on cEEG data which is not routinely available in every center managing SE.

Conclusion:

This study is the first report of the predictive value of EEG features in cEEG monitoring for outcome prediction in SE since the publication of the 2012 ACNS report on Standardized Critical Care EEG Terminology. It provides class III evidence that when adjusted for clinical predictors, EEG background information gives independent information on outcome prediction as opposed to rhythmic or periodic patterns or seizure characteristics. Indeed, the presence of a posterior dominant rhythm is associated with a greater likelihood of survival. Stage II sleep patterns are associated with the likelihood of complete recovery. While STESS and etiology are confirmed as robust predictors, RPPs and seizures are not predictive of SE outcome after statistical adjustment. These findings need to be confirmed but may be important for EEG interpretation and daily clinical practice for critically ill patients in SE.

Summary:

- Rhythmic or periodic patterns (RPP) on cEEG are present in more than half the patients after status epilepticus.
- Sixty-eight percent of cEEG recordings show definite seizures with half of seizures being purely electrographic.
- EEG background provides independent information regarding outcome after adjustment for relevant clinical findings, as compared to RPP or seizures.
- The presence of a posterior dominant rhythm is associated with a greater likelihood of survival
- Normal stage II sleep patterns are associated with the likelihood of complete recovery.

Acknowledgments:

The investigators would like to thank Christine Staehli, RN (CHUV), Christine Scott, R Tech (MGH) and the EEG fellows from the EEG laboratories at the BWH (Swapna Putta & Hong Yu), BIDMC (Andrew Schomer & Stephen VanHaerents), CHUV (Muriel Tschirren, Spyridoula Tsetsou, Myriam Guidon, Anita Barbey) and MGH (Kheder Amar, Yuan Fan, Arash Hadipour Niktarash, Lidia Moura, Marcus Ng, Deirdre O'Rourke & Sandipan Pati) for their help in patient identification and data collection.

Disclosures:

- Dr. Alvarez is funded by the Swiss National science Foundation, grant: P2GEP3_148510 and the Gottfried und Julia Bangerter-Rhyner Foundation.
- Dr. M Brandon Westover has received research funding from the American Brain Foundation.
- Dr. Barbara A. Dworetzky has received research funding from the F.D.A, the Epilepsy Foundation, and the American Epilepsy Society. She is a consultant for Sleep Med., and Best Doctors.
- Dr. Jong W. Lee has received research funding from UCB, Inc, the Duke Clinical Research Institute, and Sunovion, Inc.
- Dr Drislane has no disclosures with regard to this work.

Required statement:

Our work described here is consistent with the Journal's guidelines for ethical publication

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Tables:

Table 1:Clinical and seizures characteristics based on rhythmic and periodic patterns

	Total	No RPP	PD	RDA	SW	p-value (test)
n	120	49 (40.8%)*	45 (37.5%)*	20 (16.67%)*	6 (5%)*	
Age (mean, SD)	58.18 (16.65%)	51 (14.5%)**	61 (16.43%)**	66.25 (15.33%)**	63.5 (20.8%)	**<0.001** (ANOVA)
Male gender (n, %)	56 (46.7%)	22 (44.9%)	19 (42.2%)	12 (60%)	3 (50%)	0.62 (Fisher)
Premorbid seizures (n, %)	62 (51.6%)	27 (57.1%)	23 (51.11%)	7 (35%)	5 (83.3%)	0.19 (Fisher)
STESS (median, range)	2 (0 – 6)	2 (0 – 5)	2 (0 – 6)	3 (0 – 6)	2.5 (0 – 6)	0.45 (Kruskal-Wallis)
Potentially fatal etiology (n,%)	62 (52.1%)	21 (42.86%)	26 (59.09%)	14 (70%)	1 (16.67%)	**0.043** (χ^2)
Structural lesion (n, %) (116 with brain imaging)						
No lesion	33 (28.45%)	22 (47.83%)	6 (13.33%)	3 (15%)	2 (40%)	
Acute	40 (34.48%)	12 (26.09%)	17 (37.78%)	10 (50%)	1 (20%)	
Remote	43 (37.07%)	12 (26.09%)	22 (48.89%)	7 (35%)	2 (40%)	**0.009** (χ^2)
Definite seizure (n, %)						
Presence of definite seizure	82 (68.33%)	25 (51.02%)	36 (80%)	16 (80%)	5 (83.33%)	**0.01** (Fisher)
With clinical manifestations	42 (51.22%)	15 (60%)	14 (38.89%)	10 (62.5%)	3 (60%)	
Electrographic seizure only	40 (48.78%)	10 (40%)	22 (61.11%)	6 (37.5%)	2 (40%)	0.27 (χ^2)

Abbreviations: RPP: periodic and rhythmic pattern; RDA: rhythmic delta activity; SD: standard deviation; STESS: Status Epilepticus Severity Score; SW: spike-and-wave.
*: Row percentage
**: Column percentage
In Bold: statistically significant

Table 2: Periodic and rhythmic pattern characteristics according to their modifiers

	Total	PD	RDA	SW	P value (test)
Periodic pattern details:	71	45 (63.38%)*	20 (28.16%)*	6 (8.45%)*	
Main term					
Lateralized	51 (71.83%)**	36 (80%)**	13 (65%)**	2 (33.3%)**	
Generalized	18 (25.35%)	7 (15.6%)	7 (35%)	4 (66.7%)	
Multifocal	0	0	0	0	
Bilateral Independent	2 (2.82%)	2 (4.4%)	0	0	0.051 (χ^2)
Prevalence					
Continuous (>90%)	29 (40.85%)	21 (46.67%)	4 (20%)	4 (66.7%)	
Abundant (50-89%)	17 (23.94%)	12 (26.67%)	5 (25%)	0	
Frequent (10-49%)	17 (23.93%)	10 (22.2%)	6 (30%)	1 (16.67%)	
Occasional (1-9%)	7 (9.86%)	2 (4.44%)	5 (25%)	0	
Rare	1 (1.41%)	0	0	1 (16.67%)	**0.003** (χ^2)
Duration (for non-continuous PDs or seizures)	42	24	16	2	
Very Long (> 1 hour)	4 (9.09%)	3 (12.5%)	0	0	
Long (5 - 59 min)	13 (29.55%)	10 (41.67%)	3 (18.75%)	0	
Intermediate (1 – 4.9 min)	11 (25%)	7 (29.17%)	4 (25%)	0	
Brief (10 – 59 sec)	9 (20.45%)	4 (16.67%)	5 (31.25%)	0	
Very brief (< 10 sec)	7 (15.91%)	0	4 (25%)	2 (100%)	**0.006** (χ^2)
Frequency (median, range)	1 (<0.5 - 3.5)	1 (<0.5 – 3)	2 (0.5 - 3.5)	2.75 (1.5-3.5)	**<0.001** (Kruskal-Wallis)
Sharpness (for PD & SW only)	51				
Spiky	17 (33.3%)	11 (24.4%)	-	6 (100%)	
Sharp	33 (64.71%)	33 (73.3%)	-	0	
Sharply contoured	0	0	-	0	
Blunt	1 (1.96%)	1 (2.2%)	-	0	Not assessed
"Plus Modifiers" (for PD & RDA only)	65				
None	39 (60%)	28 (62.22%)	11 (55%)	-	
Fast activity	12 (18.46%)	12 (26.67%)	0	-	
Rhythmic activity (for PD only)	4 (6.15%)	4 (8.89%)	-	-	
Sharp component (for RDA only)	9 (13.85%)	-	9 (45%)	-	
Fast and Rhythmic activity (for PD)	1 (1.54%)	1 (2.22%)	-	-	
Fast activity and sharp (for RDA)	0	-	0	-	Not assessed
Triph. Morph. (for PD only)		2 (4.65%)	-	-	

Abbreviations: PP: periodic pattern; RDA: rhythmic delta activity; SD: standard deviation; STESS: Status Epilepticus Severity Score; SW: spike-and-wave; Triph. Morph: triphasic morphology.
*: Row percentage
**: Column percentage
In Bold: statistically significant

Table 3: cEEG features according to the 2012 ACNS Standardized Critical Care EEG Terminology, clinical characteristics and etiology and their association with mortality (univariate analysis and after logistic regression).

	Univariate Analysis:			Multivariate Analysis:		
	Non-survivors	**Survivors**	**p value (test)**	**OR**	**95% CI**	**p**
1. EEG:	n=18	n=102				
A. Rhythmic and Periodic patterns:						
Main term						
No rhythmic and periodic pattern	6 (33.3%)*	44 (43.14%)*				
LPD (incl. BiPD)	5 (25.78%)	33 (32.35%)				
GPD	1 (5.56%)	5 (4.9%)				
LRDA	0	13 (12.75%)				
GRDA	5 (27.78%)	2 (1.96%)				
LSW	0	2 (1.96%)				
GSW	1 (1.56%)	3 (2.94%)	0.002** (χ^2)	NS		
Prevalence	n=12	n=59				
Continuous (>90%)	5 (41.67%)	24 (40.68%)				
Abundant (50-89%)	4 (33.33%)	13 (22.03%)				
Frequent (10-49%)	2 (16.67%)	15 (25.42%)				
Occasional (1-9%)	1 (8.33%)	6 (10.17%)				
Rare	0	1 (1.69%)	0.87 (χ^2)	-		
Frequency	1.25 (0.5 – 3)	1 (<0.5 - 3.5)	0.33 **(**Wilcoxon)			
B. Seizures:						
Presence of seizure	13 (72.22%)	69 (67.65%)	0.79 (Fisher)	**-**		
Seizure Type						
With clinical manifestations	7 (53.85%)	35 (57.72%)				
Electrographic seizures only	6 (46.15%)	34 (49.28%)	1 (Fisher)	-		
Number of seizures/hour	2.5 (0.04 – 30)	2.43 (0.04 – 50)	0.51 **(**Wilcoxon)	-		
C. Background:						
PDR						
Present	1 (5.56%)	47 (46.08%)	0.001**(χ^2)	0.1	0.01 – 0.83	0.033
Frequency						
Alpha or more	2 (11.1%)	41 (40.2%)				
Theta	8 (44.4%)	44 (43.14%)				
Delta	8 (44.4%)	17 (16.67%)	0.01** (Fisher)	NS		
Stage II sleep transients						
Present	2 (11.11%)	31 (30.39%)				
Present abnormal	0	7 (6.86%)				
Absent	16 (88.89%)	64 (62.75%)	0.113 (Fisher)	-		
Reactivity						
Clear background reactivity	6 (33.3%)	66 (64.71%)	0.018** (Fisher)	NS		
2. STESS	4 (1 - 6)	2 (0 – 6)	0.0018** (Wilcoxon)	1.48	1.06 – 2.05	0.02
3. Potentially fatal etiology	15 (83.33%)	47 (46.53%)	0.004** (Fisher)	NS		

*: Column percentage

**: Used in regression model because p<0.05 in univariated analysis.

Abbreviation: BiPD: bilateral independent periodic discharge; CI: confidence intervals; GPD: generalized periodic discharge; GRDA: generalized rhythmic delta activity; GSW: generalized spike-and-wave; LPD: lateralized periodic discharge; LRDA: lateralized rhythmic delta activity; LSW: lateralized spike-and-wave; NS: non-significant; OR: odds ratio; STESS: STatus Epilepticus Severity Score; uV: micro volts.

Table 4: cEEG features according to the 2012 ACNS Standardized Critical Care EEG Terminology and clinical characteristics and etiology and their association with a complete clinical recovery at hospital discharges (univariate analysis and after logistic regression).

	Univariate Analysis:			Multivariate Analysis:		
	Complete recovery	**New morbidity or death**	**p value (test)**	**OR**	**95% CI**	**p**
1. EEG:	n=39*	n=81*				
A. Rhythmic and Periodic patterns:						
Main term						
No rhythmic or periodic pattern	24 (61.54%)	26 (32.1%)				
LPD (incl. BiPD)	7 (17.95%)	31 (38.27%)				
GPD	2 (5.13%)	4 (4.94%)				
LRDA	2 (5.13%)	11 (13.58%)				
GRDA	0	7 (8.64%)				
LSW	1 (2.56%)	1 (1.23%)				
GSW	3 (7.69%)	1 (1.23%)	**0.007**** (χ^2)	NS		
Prevalence	n=15	n=56				
Continuous (>90%)	6 (40%)	23 (42.07%)				
Abundant (50-89%)	4 (26.67%)	13 (23.21%)				
Frequent (10-49%)	3 (20%)	14 (25%)				
Occasional (1-9%)	1 (6.67%)	6 (10.71%)				
Rare	1 (6.67%)	0	0.39 (χ^2)	-		
Frequency	0.5 (<0.5 – 3.5)	1 (<0.5 – 3.5)	0.47 (Wilcoxon)	-		
B. Seizures:						
Presence of seizure	21 (53.85%)	61 (75.31%)	0.022** (Fisher)	NS		
Seizure Type						
With clinical manifestations	13 (61.9%)	29 (47.54%)				
Electrographic szs only	8 (38.1%)	32 (53.46%)	0.31 (Fisher)	-		
Number of seizures/hour	1.125 (0.04 – 20)	2.75 (0.04 – 50)	0.29 (Wilcoxon)	-		
C. Background:						
PDR						
Present	25 (64.1%)	23 (28.4%)	**<0.001**** (Fisher)	NS		
Frequency						
Alpha or more	19 (48.72%)	24 (29.63%)				
Theta	15 (38.46%)	37 (45.68%)				
Delta	5 (12.82%)	20 (24.69%)	0.096 (Fisher)	-		
Stage II sleep transients						
Present	22 (56.41%)	11 (13.58%)				
Present abnormal	1 (2.56%)	6 (7.41%)				
Absent	16 (41.13%)	64 (79.1%)	**<0.001**** (Fisher)	2.59	1.4 – 4.77	0.002
Reactivity						
Clear background reactivity	28 (71.79%)	44 (54.32%)	0.076 (Fisher)	-		
2. STESS	2 (0 – 3)	3 (0 – 6)	**<0.001**** (Wilcoxon)	0.51	0.32 – 0.82	0.005
3. Potentially fatal etiology	7 (17.95%)	55 (68.75%)	**<0.001**** (Fisher)	0.12	0.03 – 0.4	0.001

*: Column percentage

**: Used in regression model because p<0.05 in univariated analysis.

Abbreviation: BiPD: bilateral independent periodic discharge; CI: confidence intervals; GPD: generalized periodic discharge; GRDA: generalized rhythmic delta activity; GSW: generalized spike-and-wave; LPD: lateralized periodic discharge; LRDA: lateralized rhythmic delta activity; LSW: lateralized spike-and-wave; NS: non-significant; OR: odds ratio; STESS: STatus Epilepticus Severity Score; uV: micro volts.