



# Determinants and outcome of repeat continuous electroencephalogram monitoring—A case-control study

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## Abstract

**Objective:** A retrospective, single-center study to analyze the determinants of a repeat continuous EEG (cEEG) monitoring during hospitalization and its outcomes using a matched case-control study design.

**Methods:** Adults with a repeat cEEG session (cases) were matched by age ( $\pm 3$  years), gender, and mental status to patients with a single cEEG (controls) during hospitalization. Several clinical and EEG characteristics were analyzed to identify predictors of repeat cEEG. Repeat cEEG outcomes were analyzed based on its yield of electrographic seizure. We investigated the predictors of finding increased epileptic potential (degree of association with electrographic seizures) on the repeat cEEG, a marker for possible anti-epileptic drugs (AEDs) management change.

**Results:** A total of 213 (8.6% of all unique cEEG patients) cases were included. A multivariable conditional logistic regression model comparing cases and controls showed that the presence of acute brain insult [odds ratio (OR) = 3.36, 95% CI = 1.26-8.94,  $P = .015$ ], longer hospital admission (OR = 1.11, 95% CI = 1.07-1.15,  $P < .001$ ) and being on AEDs at the end of index cEEG (OR = 4.0, 95% CI = 1.8-8.87,  $P < .001$ ) was determinants of a repeat cEEG. Among cases, 17 (8%) had electrographic seizures on repeat cEEG. Increased epileptic potential on repeat cEEG was noted in 34 (16%) cases. The latter is associated with change in etiology after the index cEEG ( $P = .03$ ) and duration of repeat cEEG ( $P = .003$ ) based on multivariable logistic regression model. AEDs were changed in 46 (21.6%) patients based on repeat cEEG findings.

**Significance:** Repeat cEEG is not an uncommon practice. It leads to the diagnosis of electrographic seizures in a significant percentage of patients. With the potential of impacting AED management in 16%-21% patients, it should be considered in high-risk patients suffering acute brain insults undergoing prolonged hospitalization.

## KEY WORDS

acute seizures, anti-epileptic drugs, cEEG monitoring, continuous EEG, predictors

## 1 | INTRODUCTION

Continuous EEG (cEEG) monitoring utilization has steadily increased in the last decade<sup>1,2</sup> due to its ability to identify seizures in patients without overt clinical signs or symptoms.<sup>3,4</sup> Recent studies have identified various clinical and cEEG features highly associated with the diagnosis of electrographic seizures.<sup>5–7</sup> Indeed, an EEG-based scoring system to identify high seizure risk individuals has been developed.<sup>8</sup> The benefits from cEEG, including its association with reduced in-hospital mortality<sup>2</sup> need to be balanced against its association with increased cost and duration of hospitalization.<sup>2</sup> Therefore, some studies have proposed an optimum monitoring duration required to reach <5% seizure risk for a single 72-hour cEEG session.<sup>9,10</sup> However, critically ill patients may have complicated hospital courses causing prolonged hospital stays.<sup>11</sup> These patients may require more than one cEEG session during their hospitalization. A piece of indirect evidence for such practice is available from one of the largest studies on cEEG, which analyzed 5742 sessions of cEEG performed on 4773 adults at three academic centers.<sup>5</sup> The scope of repeat cEEG during a single hospitalization has not been explored yet. The aim of our current study is to fill this knowledge gap along with the following: (a) identifying the risk factors that predispose patients to undergo a repeat cEEG monitoring; (b) the yield (electrographic seizures) of repeat cEEG monitoring and (c) predictors of finding increased epileptic potential on a repeat cEEG, a marker for possible anti-epileptic drugs (AEDs) management change.

## 2 | METHODS

After IRB approval, we used our prospectively maintained cEEG database to identify adults ( $\geq 18$  years of age) who were started on cEEG monitoring 2–30 days after the completion of an index cEEG during the 2015 calendar year. The 2-day minimum time period criterion between repeat cEEGs was chosen to prevent inclusion of patients whose cEEG monitoring is temporarily discontinued due to imaging or surgical procedures. These patients are typically restarted on cEEG within 24 hours ( $\leq 1$  day). The 30 days maximum time period criterion was chosen because of increased chances of such late repeat cEEG to occur during readmission. Patients identified by the above search were reviewed, and the ones undergoing repeat cEEG during readmission were excluded. The remaining patients (“cases”) were included in the final analysis. We matched (1:1) the cases based on age ( $\pm 3$  years), gender, and mental status (defined as awake, lethargy, stupor, or coma) at the start of index cEEG to patients who did not undergo a repeat cEEG

### Key Points

- Close to 1 in 10 patients (8.6%) may undergo a repeat continuous EEG (cEEG) monitoring session during the same hospitalization
- Determinants of a repeat cEEG, compared to matched controls: presence of an acute brain insult, longer hospitalization, AEDs at the end of index cEEG
- Repeat cEEG session identified electrographic seizure in 8% patients and 34 (16%) had increased epileptic findings, including 11 first time seizures
- Almost 1 in 5 patients (21.6%) had an AED management change (initiation/addition of an AED) based on repeat cEEG findings
- Repeat cEEG session should not be withheld when indications persist/arise, irrespective of index cEEG findings or AED status

monitoring (“controls”) during the same calendar year. In scenarios with more than one control fulfilling above criteria, the one closest in age to the case was included in the study. Clinical or EEG outcomes were not considered in the selection of controls.

### 2.1 | Clinical variables

Identification of cases and controls was followed by the review of electronic health records (EHR) to extract clinical variables. This included demographical data, total duration of hospital admission (days), history of epilepsy, patient location at time of index cEEG [Neuro (neurological medical-surgical floor or neuro-intensive care unit) vs Non-Neuro (rest of the hospital)], duration of index cEEG session (in days) and anti-epileptic drugs (AEDs) status at the end of index cEEG. In the control group, AEDs were withdrawn in some patients by the end of index cEEG due to change in the goals of care (hospice transfer or withdrawal of care). They are classified such in the results section and excluded from statistical modeling of predictors for repeat cEEG (see below). Primary etiology associated with cEEG findings was classified as acute brain insult (within preceding 7 days of start of cEEG monitoring; eg stroke, hemorrhage etc), progressive brain insult (eg tumors), anoxic brain insult, toxic/metabolic/infectious encephalopathy (T/M/I encephalopathy—diagnosed when reversal of such etiology led to improvement in altered mental status), epilepsy (if breakthrough seizures led to the hospitalization of people with epilepsy), and miscellaneous (not classifiable in any of the above category including autoimmune/paraneoplastic encephalitis). Patients who had concomitant T/M/I encephalopathy along with acute brain insult were categorized in the latter category. Indications for performing

cEEG were classified as altered mental status [AMS, suspected to be caused by non-convulsive seizure/status epilepticus (NCS/NCSE); labeled as “AMS” in the results section], “seizure-like event” (episodes concerning for clinical seizures or paroxysmal, mostly motor, events like myoclonic jerks or transient unilateral posturing in comatose patients) or as part of hypothermia protocol among patients who suffered cardiac arrest. Patients with AMS after a witnessed clinical seizure were categorized under “seizure-like event” category.

For the study aim 2b, we collected variables including days between the index and repeat cEEG, duration of repeat cEEG (in days), indication for repeat cEEG, change in etiology since the end of index cEEG and changes in management (AED regimen).

## 2.2 | Continuous EEG variables

The cEEG database was used to identify the primary EEG findings for controls and cases (index and repeat cEEG). Raw cEEG tracings were not re-reviewed for the purpose of this research project because the plan was to analyze the real world factors influencing repeat cEEGs. Only a single primary cEEG finding was classified for sessions with multiple findings. It was determined as the EEG finding that is highest on the listed spectrum (based on their association with acute seizures): non-epileptogenic (theta/delta slowing) findings <isolated interictal epileptiform discharges (IEDs) (eg sharp waves, spikes)<sup>12</sup> <generalized periodic discharges (GPDs)<sup>13</sup> <lateralized periodic discharges (LPDs, formerly PLEDs)<sup>14</sup>/lateralized rhythmic delta activity (LRDA)<sup>15</sup> <electrographic seizure (classified based on Salzburg criteria<sup>16</sup>). Repeat cEEG sessions were classified as having “increased epileptic potential” if the repeat session revealed a primary finding that was higher on the abovementioned spectrum compared to their index cEEG. Due to the unclear significance of GPDs in different etiological settings, specially encephalopathies, and our evolving understanding of them,<sup>17</sup> index cEEG sessions with only GPDs ( $\pm$  theta/delta slow) that did not qualify for electrographic seizure per Salzburg criteria,<sup>16</sup> were not considered potentially epileptic. While determining increased epileptic potential, we did not consider patients with primarily non-epileptogenic findings on index cEEG showing only GPDs on the repeat cEEG session due to abovementioned reason.

## 2.3 | Statistical methods

Continuous measures were summarized with Median [Q1, Q3], and categorical factors were summarized with frequencies and percentages. Comparisons between cases and controls for continuous measures were analyzed using the Wilcoxon signed-rank test. Wilcoxon signed-rank test was chosen as the alternative to a paired t test because the continuous measures were not normally distributed (verified by the Shapiro-Wilk

test for normality). Unordered matched categorical data with two categories (eg Yes vs No) were analyzed with McNemar's test; Bowker's test was used to analyze matched data with three or more categories. Pearson's Chi-square test was used to analyze non-matched categorical data [“increased epileptic potential” (yes vs no) for patients with repeat cEEG]. Multivariable conditional logistic regression was used to identify and analyze the determinants of a patient undergoing a repeat cEEG. For this analysis, patients (and their matches) with “Poor prognosis” for AED status after cEEG, were removed. Multivariable logistic regression was used to predict the outcome “increased epileptic potential” on repeat cEEG. To identify predictors, backwards selection procedures were used for model selection. Receiver operating characteristic (ROC) analysis was used to identify a threshold for dichotomizing continuous variables for the regression analysis. *P*-values under .05 were considered statistically significant for the analysis. The analysis was done in SAS software (version 9.4).

## 3 | RESULTS

### 3.1 | Repeat cEEG population

A total of 213 patients [median age 64 (53-73) years; 52.6% females] underwent repeat cEEG monitoring during a single hospitalization. As noted in Supplemental Figure S1, they accounted for 8.6% of the total unique patients monitored during the study period. A total of 35 (16.4%) patients had epilepsy history and underwent cEEG monitoring due to breakthrough seizures. The most common etiology was acute brain insults (46.9% patients) followed by T/M/I encephalopathy (17.4%). The indication for cEEG monitoring in 65.3% of patients was AMS. Almost two-thirds (64.3%) of patients undergoing repeat cEEG were being taken care on a neurological floor in the hospital at the time of index cEEG. Thirty-five (16.4%) cases were found to have electrographic seizures, and an additional 46 (21.6%) patients had potentially epileptic findings on the index cEEG. At the end of index cEEG, 65.7% of the cases were on AEDs.

### 3.2 | Determinants of repeat cEEG

The cases and controls were well matched by age, gender, and mental status (Table 1). The median duration of index cEEG monitoring was 2 days in both groups but was significantly longer among cases ( $P = .01$ ). Univariate analysis showed that the two groups differed by underlying etiology ( $P < .001$ ), cases had a much prolonged hospitalization (25 vs 7 days,  $P < .001$ ), were provided care on a neurological floor ( $P < .001$ ), and were on an AED at the end of cEEG ( $P < .001$ ) (Table 1). Among controls, 37 (17.4%) patients who were on AEDs were withdrawn from AEDs by the end of index cEEG due to change in goals of care. The cases and controls did not differ significantly in the identification of electrographic

**TABLE 1** Total study population characteristics and comparison of “Cases” and “Controls”

Variables	Total (N = 426)	Control (N = 213)	Case (N = 213)	P-value
Age, Median [Q1, Q3]	64.0 [54.0,73.0]	64.0 [53.0,73.0]	64.0 [54.0,74.0]	.814 <sup>b</sup>
Gender, No. (%)				
Female	224 (52.6)	112 (52.6)	112 (52.6)	1
Male	202 (47.4)	101 (47.4)	101 (47.4)	
Mental status, No. (%)				
Awake	124 (29.1)	62 (29.1)	62 (29.1)	1
Coma	56 (13.1)	28 (13.1)	28 (13.1)	
Lethargy	126 (29.6)	63 (29.6)	63 (29.6)	
Stupor	120 (28.2)	60 (28.2)	60 (28.2)	
Duration of hospital stay, Median [Q1, Q3]	15.0 [7.0,28.0]	7.0 [4.0,16.0]	25.0 [15.0,36.0]	<b>&lt;.001<sup>a</sup></b>
Epilepsy history, No. (%)	71 (16.7)	36 (16.9)	35 (16.4)	.886 <sup>b</sup>
Etiology, No. (%)				
Acute brain insult	162 (38.0)	62 (29.1)	100 (46.9)	<b>&lt;.001<sup>c</sup></b>
Anoxic brain insult	37 (8.7)	23 (10.8)	14 (6.6)	
Epilepsy	62 (14.6)	27 (12.7)	35 (16.4)	
Miscellaneous	39 (9.2)	31 (14.6)	8 (3.8)	
Progressive brain insult	35 (8.2)	16 (7.5)	19 (8.9)	
T/M/I Encephalopathy	91 (21.4)	54 (25.4)	37 (17.4)	
cEEG indication, No. (%)				
AMS	271 (63.6)	132 (62.0)	139 (65.3)	.402 <sup>c</sup>
Hypothermia protocol	30 (7.0)	19 (8.9)	11 (5.2)	
Seizure-like event	125 (29.3)	62 (29.1)	63 (29.6)	
Patient location, No. (%)				
Neuro floor	238 (55.9)	101 (47.4)	137 (64.3)	<b>&lt;.001<sup>b</sup></b>
Non-neuro floor	188(44.1)	112 (52.6)	76 (35.7)	
Duration of First cEEG, Median [Q1, Q3]	2.0 [1.00,3.0]	2.0 [1.00,3.0]	2.0 [1.00,4.0]	<b>.010<sup>a</sup></b>
AED status after cEEG, No. (%)				
No	172 (40.4)	99 (46.5)	73 (34.3)	<b>&lt;.001<sup>c</sup></b>
Poor prognosis	37 (8.7)	37 (17.4)	0 (0.0)	
Yes	217 (50.9)	77 (36.2)	140 (65.7)	
Electrographic seizures, No. (%)	61 (14.3)	26 (12.2)	35 (16.4)	.216 <sup>b</sup>
Potentially epileptic, No. (%)	74 (17.4)	28 (13.1)	46 (21.6)	<b>.022<sup>b</sup></b>

Note: Bold values = statistically significant *P*-values.

<sup>a</sup>Wilcoxon Signed Rank test

<sup>b</sup>McNemar's test.

<sup>c</sup>Bowker's test of Symmetry

seizures on cEEG [35 (16.4%) cases vs 26 (12.2%) controls; *P* = .22]. However, a significantly higher percentage of cases had potentially epileptic findings compared to controls [46 (21.6%) cases vs 28 (13.1%) controls; *P* = .02].

Multivariable conditional logistic regression (Table 2) showed that the determinants of a repeat cEEG included the presence of an acute brain insult [Odds ratio (OR) = 3.36, 95% confidence interval (CI) = 1.26-8.94, *P* = .015] compared to T/M/I encephalopathy, longer duration of hospitalization (OR = 1.11, 95% CI = 1.07-1.15, *P* < .001) and

patient being on AEDs at the end of index cEEG (OR = 4.0, 95% CI = 1.8-8.87, *P* < .001).

### 3.3 | Repeat cEEG outcomes and predictors

Cases underwent repeat cEEG after a median interval of 5 (3-9) days after the end of index cEEG. The total duration of repeat cEEG session was 2 (1-3) days. A total of 14 cases had “miscellaneous” indications for repeat cEEG (Table 3), including 11 (5.2%) patients requiring cEEG to guide safe

downtitration of AEDs and 3 patients for delayed vasospasm monitoring after subarachnoid hemorrhage. Change in etiology after index cEEG was noted in 16 patients (three cardiac arrests, five ischemic strokes, three SDH, one hemorrhagic

conversion of stroke, one posterior reversible encephalopathy syndrome and three underwent neurosurgical procedure).

A total of 17 (8%) patients were found to have electrographic seizures on repeat cEEG (individual data in Table 5). Eleven (5.2% of total cases) did not have seizures on their index cEEG. As noted in Table 5, 82.3% (14/17) found to have electrographic seizure underwent repeat cEEG for indication of seizure-like events. Overall, among the 67 patients who underwent repeat cEEG due to seizure-like events, 53 (79.1%) were not eventually diagnosed with electrographic seizure. The increased epileptic potential was noted in 34 (16%) patients, including the 11 patients with newly diagnosed seizure. Figure 1 shows the primary cEEG findings on the index and repeats monitoring of the 34 patients with increased epileptic potential.

Univariate analysis comparing patients with increased epileptic potential on repeat cEEG to the rest of cases (Table 3) showed that they were more likely to have seizure-like event prompting repeat cEEG ( $P < .002$ ), a change in etiology since index cEEG ( $P < .015$ ) and their repeat cEEG was significantly longer (median 3.5 vs 2 days;  $P < .001$ ). Factors predicting an increased epileptic potential of repeat cEEG, based on multivariable logistic regression, included a change in etiology after index cEEG [OR = 3.54 (1.14-10.97);  $P = .029$ ] along with a longer duration of monitoring [OR = 1.2 (1.06-1.36);  $P = .003$ ] (Table 4). Days between the repeat cEEGs was not found to be a significant predictor of increased epileptic potential on ROC analysis ( $P$ -value = .371).

A total of 46 (21.6%) patients had a change in AED management (initiation of an AED/addition of another

**TABLE 2** Multivariable conditional logistic regression results for predicting a repeat cEEG

Variables	Odds Ratio Estimate	95% Confidence Interval		P-value
Hospital duration of stay	1.106	1.069	1.145	<b>&lt;.001</b>
Final etiology				
Acute (vs T/M/I Encephalopathy)	3.362	1.264	8.938	<b>.015</b>
Anoxic (vs T/M/I Encephalopathy)	0.901	0.223	3.650	.884
Epilepsy (vs T/M/I Encephalopathy)	2.045	0.589	7.103	.260
Miscellaneous (vs T/M/I Encephalopathy)	0.195	0.033	1.144	.070
Progressive (vs T/M/I Encephalopathy)	0.885	0.157	4.994	.890
AED status after cEEG				
Yes (vs No)	3.998	1.803	8.863	<b>&lt;.001</b>

Note: Bold values = statistically significant  $P$ -values.

**TABLE 3** Repeat cEEG characteristics and comparison of patients found to have increase in epileptic potential compared to index cEEG ("Yes" sub-group) and the rest ("No" sub-group)

Variables	Total (N = 213)	No (N = 179)	Yes (N = 34)	P-value
Days between two cEEG, Median [Q1, Q3]	5.0 [3.0,9.0]	5.0 [3.0,9.0]	5.0 [3.0,13.0]	.360 <sup>a</sup>
Duration of repeat cEEG, Median [Q1, Q3]	2.0 [1.00,3.0]	2.0 [1.00,3.0]	3.5 [2.0,6.0]	<b>.001<sup>a</sup></b>
Mental status, No. (%)				
Awake	51 (23.9)	40 (22.3)	11 (32.4)	.18 <sup>b</sup>
Coma	22 (10.3)	18 (10.1)	4 (11.8)	
Lethargy	79 (37.1)	72 (40.2)	7 (20.6)	
Stupor	61 (28.6)	49 (27.4)	12 (35.3)	
Indication for repeat cEEG, No. (%)				
AMS	132 (62.0)	117 (65.4)	15 (44.1)	<b>.002<sup>b</sup></b>
Miscellaneous	14 (6.6)	14 (7.8)	0 (0.0)	
Seizure-like event	67 (31.5)	48 (26.8)	19 (55.9)	
Change in location, No. (%)	37 (17.4)	28 (15.6)	9 (26.5)	.127 <sup>b</sup>
Change in etiology, No. (%)	16 (7.5)	10 (5.6)	6 (17.6)	<b>.015<sup>b</sup></b>
Change in management, No. (%)	46 (21.6)	28 (15.6)	18 (52.9)	<b>&lt;.001<sup>b</sup></b>

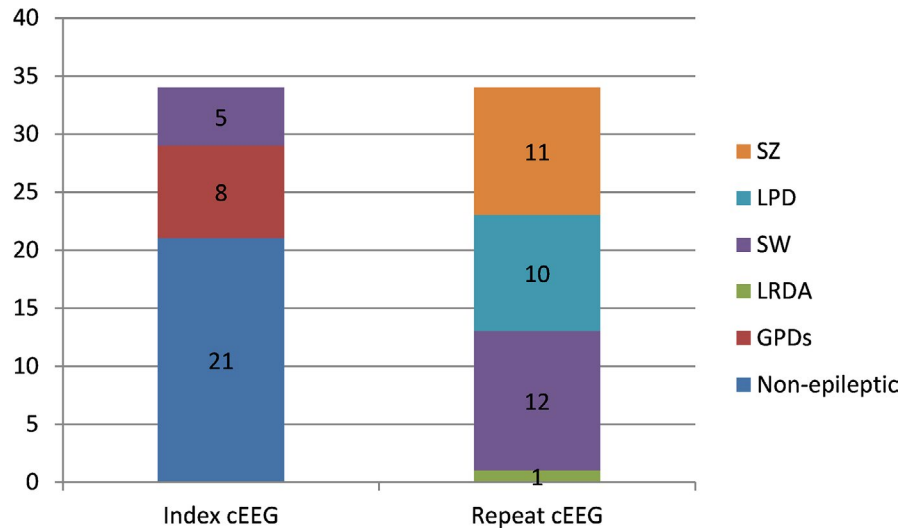
Note: Bold values = statistically significant  $P$ -values

<sup>a</sup> = Wilcoxon signed-rank test.

<sup>b</sup> = Pearson's chi-square test.



**FIGURE 1** cEEG findings of index and repeat cEEGs for patients with increased epileptic potential on the repeat cEEG. GPDs, generalized periodic discharges; LPDs, lateralized periodic discharges; LRDA, lateralized rhythmic delta activity; SW, sharp waves; SZ, seizures



AED) based on repeat cEEG findings. More than half (52.9%) of the patients with a higher epileptic potential on repeat cEEG had a change in their AED management, which was significantly higher [OR = 6.07 (2.77-13.3); *P* < .001] than patient lacking such findings on repeat cEEG.

#### 4 | DISCUSSION

Our study shows that close to 1 in 10 patients requiring cEEG may undergo a repeat evaluation during the same hospitalization. During the repeat cEEG monitoring, 8% were found to have electrographic seizures. This figure is not too different from 12.5% of 5742 cEEG sessions found to have a seizure in a recent multi-center study.<sup>5</sup> Notably, most patients with a seizure on repeat cEEG did not have seizures during their index cEEG monitoring. These findings signify that a repeat cEEG during a hospital admission is not uncommon and leads to a diagnosis of seizures in a small, but significant number of patients.

The comparison of repeat cEEG patients with age, gender, and mental status matched patients undergoing a single cEEG session showed that the odds for a repeat evaluation increases 1.1 times for each extra day of stay in

the hospital. At the end of index cEEG, of note, a sizable percentage of controls (17.4%) had a withdrawal of care or transfer to hospice due to change in goals of care. When these patients are excluded from the analysis, it seems that the odds of a repeat cEEG are higher in patients who have a more prolonged, complicated hospitalization. The repeat EEG in these patients may be due to an unresolved indication for index cEEG like altered mental status (noted in 62% of cases at the time of index and repeat cEEG). Other predictors of a repeat cEEG were the underlying etiology and AED status at the end of index cEEG. Patients requiring repeat cEEG were three times more likely to have suffered acute brain insults compared to systemic issues (T/M/I encephalopathy; chosen as reference as rest of the etiological groups directly impact the brain). While this is not surprising, an almost 4 times higher likelihood of a repeat cEEG among patients who are on AEDs at the end of index cEEG may seem counterintuitive. However, it is likely a marker of higher suspicion for seizures in those patients, warranting AED treatment at the time of index cEEG and then, a subsequent lower threshold for repeating the cEEG. This assertion is supported by a significantly greater percentage of cases having potentially epileptic findings on index cEEG compared to controls (21.6% vs 13.1%). The lack of difference in percentage of cases and controls with electrographic seizure is reflective of the baseline risk of seizure in patients with acute hospitalization with systemic or central insults.

It may be argued that a repeat cEEG is required in some patients because of a shorter than the indicated duration of index cEEG. This is not the case as shown by a significantly longer (*P* = .01) index session among repeat cEEG patients compared to the controls. Cases had the index cEEG for a median of 2 days – a time duration sufficient to obtain a <5% seizure risk in patients during a single cEEG session.<sup>9</sup>

**TABLE 4** Multivariable logistic regression for predictors of increased epileptic potential on repeat cEEG

Factor	Odds Ratio Estimate	95% Confidence Interval	<i>P</i> -value
Duration of repeat cEEG	1.203	1.067 1.358	.003
Change in etiology			
Yes (vs No)	3.538	1.141 10.972	<b>.029</b>

Note: Bold values = statistically significant *P*-values

**TABLE 5** Demographical and clinical details of the patients found to have seizures on repeat cEEG

No	Age, Gender	Mental status (index cEEG)	Indication (index cEEG)	Etiology	Prominent index cEEG finding	AED at end of index cEEG	Days b/w 2 cEEG	Change in etiology	Mental status at repeat cEEG	Indication (repeat)
1	62, M	Stupor	AMS	T/M/I Encephalopathy	GPDs	No	4	No	Awake	Seizure-like event
2	55, M	Lethargy	Seizure-like event	Epilepsy	Seizures	Yes	11	No	Awake	Misc
3	27, M	Lethargy	AMS	Epilepsy	Seizures	Yes*	12	No	Lethargy	Seizure-like event
4	56, F	Coma	Seizure-like event	Acute	Seizures	Yes	6	No	Stupor	Seizure-like event
5	59, F	Awake	AMS	Epilepsy	Seizures	Yes	29	No	Awake	Seizure-like event
6	67, M	Lethargy	Seizure-like event	Misc	Seizures	Yes	8	No	Lethargy	Seizure-like event
7	70, M	Awake	Seizure-like event	T/M/I Encephalopathy	Seizures	Yes	5	b/l Hygroma	Awake	Seizure-like event
8	63, M	Lethargy	AMS	Progressive	CS	No	9	No	Stupor	AMS
9	37, F	Awake	Seizure-like event	Epilepsy	SW	Yes	4	No	Awake	Seizure-like event
10	51, M	Lethargy	AMS	Epilepsy	GPDs, SW	Yes	17	No	Coma	Seizure-like event
11	55, M	Awake	Seizure-like event	T/M/I Encephalopathy	CS	No	21	No	Awake	Seizure-like event
12	71, F	Coma	AMS	T/M/I Encephalopathy	GPDs	No	25	No	Awake	Seizure-like event
13	78, M	Lethargy	AMS	Acute	SW	No	4	No	Coma	Seizure-like event
14	59, M	Awake	Seizure-like event	Acute	CS	Yes	10	New SDH	Awake	Seizure-like event
15	67, F	Lethargy	AMS	Progressive	CS	Yes	2	Postmeningioma resection	Stupor	AMS
16	62, M	Lethargy	AMS	Acute	CS	No	7	PRES	Stupor	Seizure-like event
17	68, F	Stupor	Hypothermia protocol	Anoxic brain insult	GPDs	No	23	Stroke	Coma	Seizure-like event

\*Home AEDs.

One of the most significant findings of our study is that repeat cEEG may impact the management of a high percentage of patients. Almost 1 in 5 patients (21.6%) undergoing repeat cEEG had a change in AED management based on its findings. Interestingly, 5% of repeat cEEGs were performed for the specific indication of safely weaning down AEDs in high seizure risk patients. There is no consensus on the AED treatment for several of the cEEG findings and consequentially, several expert opinions have been proposed.<sup>18-21</sup> There is also inter-institutional variability in the AED management of patients undergoing cEEG.<sup>22</sup> Therefore, we considered an increase in the epileptic potential of the findings on repeat cEEG, and not the change in AED management from the repeat monitoring at our institution, as a measure of its primary impact on patient care. We found that 16% of patients were noted to have findings on repeat cEEG, which were potentially more epileptic than their index cEEG. This group was six times more likely to undergo an AED change compared to patients with no increase in the epileptic potential of repeat cEEG findings. Combined, above findings suggest that cEEG can potentially impact AED management in 16%-21% of patients. It is clinically important and worthwhile to note that the duration between the two cEEG sessions did not affect the chances of a repeat cEEG being more epileptic. Rather, the odds of the latter outcome were three times higher if there was a change in etiology during the intervening period.

A total 17 (8%) repeat cEEG patients were found to have seizures, of whom two-thirds (11 out of 17; 64.7%) had negative (lacking seizures) index cEEG. This shows that despite our improved understanding of optimum duration of single cEEG sessions to confidently rule out seizures,<sup>9,10</sup> there are many patients in tertiary care centers with prolonged hospitalizations<sup>11</sup> (median 25 days among “cases”), who may have a negative index cEEG of median 2 days and still develop seizure later during the hospital course. Usually, cEEG is interpreted by a team not involved in the direct clinical care of patients undergoing monitoring. Univariate analysis showed that patients with increased epileptic findings on repeat cEEG were significantly more likely to undergo repeat cEEG due to witnessed “seizure-like event” and it was an indication in > 80% of patients found to have seizures (Table 5). This suggests that patients with prolonged hospitalization and a “negative” initial cEEG should not be denied a repeat cEEG if the treating team notices events that are clinically concerning for epileptic seizures, especially in patients with a change in etiology, irrespective of the time gap between the two cEEG sessions. In absence of repeat cEEG, treating the seizure-like events clinically could possibly have led to an over-treatment with AEDs in as much as 4 out of 5 (79.1%) such patients. Given that all paroxysmal events in critically ill

patients are not epileptic seizure, a negative repeat cEEG could lead to judicious clinical management.

There are some limitations to our study. It is a retrospective, single-center study. Future single or multi-center studies are needed to test the replicability of our results. We did not look into factors like change in treating physicians/teams over course of hospital stay that may affect the chance of repeat cEEG. We did not perform sophisticated statistical analysis to find out predictors specifically for seizures on repeat cEEG due to small number of this outcome. While a reasonable argument may be made against the choice of using “increased epileptic potential” of repeat cEEG findings as a marker of potential impact on management, we believe that it is a practical measure given lack of agreement on treatment strategy of cEEG findings. It is important to note that while the association with electrographic seizures (epileptic potential) of the individual components of the “epileptic potential” scale has been validated,<sup>5,15</sup> the proposed scale as a whole has not a validated and is only a conceptual construct. The initial seizure risk on cEEG has been shown to be dependent on the mental status and prior seizures.<sup>9</sup> Although we were able to match our cases and controls by mental status, we were not able to match them by their prior seizure status. We found that the presence of acute brain insult increases the chances of undergoing a repeat cEEG. However, our study was not designed to predict the likelihood of a repeat cEEG in patients with matched etiology. Our database search strategy excluded patients with a repeat cEEG 30 days after an index monitoring because a large majority of these patients are likely to be rehospitalizations. Although a reasonable line of inquiry, the indications and yield of a repeat cEEG during a rehospitalization are a separate research question.

In conclusion, our study shows that a small but significant number of patients with prolonged hospitalization undergo repeat cEEG monitoring. In total, 16% of repeat cEEGs reveal findings with increased epileptic potential, which may impact AED management. With 8% of repeat cEEGs revealing electrographic seizure, two-thirds of which are newly diagnosed, our findings suggest that a repeat monitoring should not be withheld in case of ongoing or newly arising indication, irrespective of index cEEG findings.

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## CONFLICT OF INTERESTS

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.



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## REFERENCES

1. Ney JP, van der Goes DN, Nuwer MR, Nelson L, Eccher MA. Continuous and routine EEG in intensive care: utilization and outcomes, United States 2005–2009. *Neurology*. 2013;81:2002–2008.
2. Hill CE, Blank LJ, Thibault D, Davis KA, Dahodwala N, Litt B, et al. Continuous EEG is associated with favorable hospitalization outcomes for critically ill patients. *Neurology*. 2019;92:e9–e18.
3. Claassen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology*. 2004;62:1743–1748.
4. Herman ST, Abend NS, Bleck TP, Chapman KE, Drislane FW, Emerson RG, et al. Consensus statement on continuous EEG in critically ill adults and children, part I: indications. *J Clin Neurophysiol*. 2015;32:87–95.
5. Rodriguez Ruiz A, Vlachy J, Lee JW, Gilmore EJ, Ayer T, Haider HA, et al. Association of periodic and rhythmic electroencephalographic patterns with seizures in critically ill patients. *JAMA Neurol*. 2017;74:181–188.
6. Newey CR, Kinzy TG, Punia V, Hantus S. Continuous Electroencephalography in the Critically Ill. *J Clin Neurophysiol*. 2018;35:325–331.
7. Punia V, Garcia CG, Hantus S. Incidence of recurrent seizures following hospital discharge in patients with LPDs (PLEDs) and nonconvulsive seizures recorded on continuous EEG in the critical care setting. *Epilepsy Behav*. 2015;49:250–254.
8. Struck AF, Ustun B, Ruiz AR, Lee JW, LaRoche SM, Hirsch LJ, et al. Association of an electroencephalography-based risk score with seizure probability in hospitalized patients. *JAMA Neurol*. 2017;74:1419–1424.
9. Struck AF, Osman G, Rampal N, Biswal S, Legros B, Hirsch LJ, et al. Time-dependent risk of seizures in critically ill patients on continuous electroencephalogram. *Ann Neurol*. 2017;82:177–185.
10. Westover MB, Shafi MM, Bianchi MT, Moura LM, O'Rourke D, Rosenthal ES, et al. The probability of seizures during EEG monitoring in critically ill adults. *Clin Neurophysiol*. 2015;126:463–471.
11. Zampieri FG, Ladeira JP, Park M, Haib D, Pastore CL, Santoro CM, et al. Admission factors associated with prolonged (>14 days) intensive care unit stay. *J Crit Care*. 2014;29:60–65.
12. Noachtar S, Binnie C, Ebersole J, Mauguière F, Sakamoto A, Westmoreland B. A glossary of terms most commonly used by clinical electroencephalographers and proposal for the report form for the EEG findings. *The International Federation of Clinical Neurophysiology. Electroencephalogr Clin Neurophysiol Suppl*. 1999;52:21–41.
13. Foreman B, Claassen J, Abou Khaled K, Jirsch J, Alschuler DM, Wittman J, et al. Generalized periodic discharges in the critically ill: a case-control study of 200 patients. *Neurology*. 2012;79:1951–1960.
14. Punia V, Vakani R, Burgess R, Hantus S. Electrographic and clinical natural history of lateralized periodic discharges. *J Clin Neurophysiol*. 2018;35:71–76.
15. Gaspard N, Manganas L, Rampal N, Petroff OA, Hirsch LJ. Similarity of lateralized rhythmic delta activity to periodic lateralized epileptiform discharges in critically ill patients. *JAMA Neurol*. 2013;70:1288–1295.
16. Beniczky S, Hirsch LJ, Kaplan PW, Pressler R, Bauer G, Aurlieu H, et al. Unified EEG terminology and criteria for nonconvulsive status epilepticus. *Epilepsia*. 2013;54(Suppl 6):28–29.
17. Sully KE, Husain AM. Generalized Periodic Discharges. *J Clin Neurophysiol*. 2018;35:199–207.
18. Chong DJ, Hirsch LJ. Which EEG patterns warrant treatment in the critically ill? Reviewing the evidence for treatment of periodic epileptiform discharges and related patterns. *J Clin Neurophysiol*. 2005;22:79–91.
19. Rubinos C, Reynolds AS, Claassen J. The ictal-interictal continuum: to treat or not to treat (and how)? *Neurocrit Care*. 2018;29:3–8.
20. Sivaraju A, Gilmore EJ. Understanding and managing the ictal-interictal continuum in neurocritical care. *Curr Treat Options Neurol*. 2016;18:8.
21. Rodriguez V, Rodden MF, LaRoche SM. Ictal-interictal continuum: A proposed treatment algorithm. *Clin Neurophysiol*. 2016;127:2056–2064.
22. Alvarez V, Rodriguez Ruiz AA, LaRoche S, Hirsch LJ, Parres C, Voinescu PE, et al. The use and yield of continuous EEG in critically ill patients: A comparative study of three centers. *Clin Neurophysiol*. 2017;128:570–578.

## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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