■ Original article

Epileptic Disord 2022; 24 (5): 1-7

Epileptic Disorders

Effect of rapid EEG on anti-seizure medication usage

Deepika Kurup[1], Zachary Davey[1], Phuong Hoang[1], Connie Wu[1], Katherine Werbaneth[2], Varun Shah[1], Karen G. Hirsch[1], Prasanthi Govindarajan[3], Kimford J. Meador[1]

[1] Department of Neurology & Neurological Sciences, Stanford University School of Medicine, Stanford, CA, USA
[2] Department of Neurology, California Pacific Medical Center, Sutter Health, San Francisco, CA, USA
[3] Department of Emergency Medicine, Stanford University, Stanford, CA USA

Received February 28, 2022;
Accepted May 21, 2022

ABSTRACT

Objective. To study how early diagnoses from rapid EEG (rEEG) during the initial evaluation of patients with suspected non-convulsive seizures correlates with changes in anti-seizure medication (ASM) use.

Methods. We performed a retrospective chart review of 100 consecutive adult patients at an academic medical center who underwent rEEG monitoring for suspected non-convulsive seizures. We collected information on the timing of ASM administration and categorized EEG diagnoses as seizures (SZ), highly epileptiform patterns (HEP), or normal or slow activity (NL/SL). We used a χ^2 test to determine whether the use of ASMs was significantly different between SZ/HEP and NL/SL cases.

Results. Of 100 patients, SZ were found in 5%, HEP in 14%, and no epileptiform/ictal activity in 81%. Forty-six percent of patients had received ASM(s) before rEEG. While 84% of HEP/SZ cases were started or continued on ASMs, only 51% of NL/SL cases were started or continued on ASMs after rEEG (χ^2 [1, n=100] = 7.09, p=0.008). Thirty-seven patients had received sedation (*i.e.*, propofol or dexmedetomidine) prior to rEEG. In 15 patients (13/30 NL/SL, 2/7 HEP/SZ), sedation was discontinued following rEEG.

Significance. Our study demonstrates that seizures were rapidly ruled out with rEEG in 81% of patients while 19% of patients were rapidly identified as having seizures or being at higher risk for seizures. The rapid evaluation of patients correlated with a significant reduction in ASM treatment in NL/SL cases compared to HEP/SZ cases. Thus, early access to EEG information may lead to more informed and targeted management of patients suspected to have non-convulsive seizures.

Key words: electroencephalography, neurocritical care, emergency medicine, healthcare cost

• **Correspondence:**
Deepika Kurup
291 Campus Drive,
Stanford, CA 94305, USA
Kimford Meador
213 Quarry Road,
MC 5979, Palo Alto,
CA 94304-5979, USA
<dkurup@stanford.edu>
<kmeador@stanford.edu>

doi:10.1684/epd.2022.1463

Electroencephalogram (EEG) is the current gold-standard method for clinical monitoring of the brain's electrophysiological activity, and provides vital diagnostic information when there is need to evaluate for non-convulsive seizures or non-convulsive status epilepticus (NCSE) [1]. Using EEG, clinicians may rule in seizures or highly abnormal activity (*i.e.*, abundant discharges or rhythmic periodic patterns) and elect to start treatment, or reduce their suspicion for seizures thereby changing their treatment decisions towards less aggressive therapies or no seizure treatment.

A recent multicenter prospective observational study [2] showed that the use of a rapid response EEG (rEEG) during initial neurological evaluation of patients with suspected non-convulsive

seizures increased physicians' diagnostic accuracy for detecting seizures and increased their confidence in their assessment and treatment decisions. Smaller trials in our own medical center [3] and in a community hospital [4] also showed that the use of rEEG led to faster acquisition of EEG and suggested that it changed physicians' decisions. However, it remains to be determined if early access to EEG diagnosis provided by rEEG is significantly associated with actual changes in the usage of anti-seizure medications (ASMs) in clinical practice. The current study was aimed at addressing this unknown. Focusing on ASM usage was motivated by the practicality and reliability of measuring this metric in our retrospective study.

Methods

This study was approved by Stanford University's Institutional Review Board. We reviewed the electronic medical records of 100 consecutive cases of adult patients (≥18 years) who were examined with rEEG by the Neurology consult team in the emergency department and intensive care unit. All patients who were evaluated with the Ceribell rEEG for any indication were included. The duration of rEEG recording was determined by the treatment team. The rEEG procedure notes were reviewed by two independent neurologists and EEG diagnoses were categorized as either: (1) normal EEG or diffuse/focal slowing (NL/SL); (2) highly epileptiform patterns (HEP); and (3) generalized or focal seizures (SZ). Cases were categorized as HEP if they included one or more patterns that did not fully meet the Salzburg criteria [5] for electrographic seizures but represented electrographic epileptiform activity (as defined in the DECIDE multicenter study [2] with the same rEEG device). These patterns included: abundant sporadic or periodic discharges with superimposed rhythmic, sharp, or fast activity. *See figure 1* for a representative sample of electrographic features on rEEG for each of these categories.

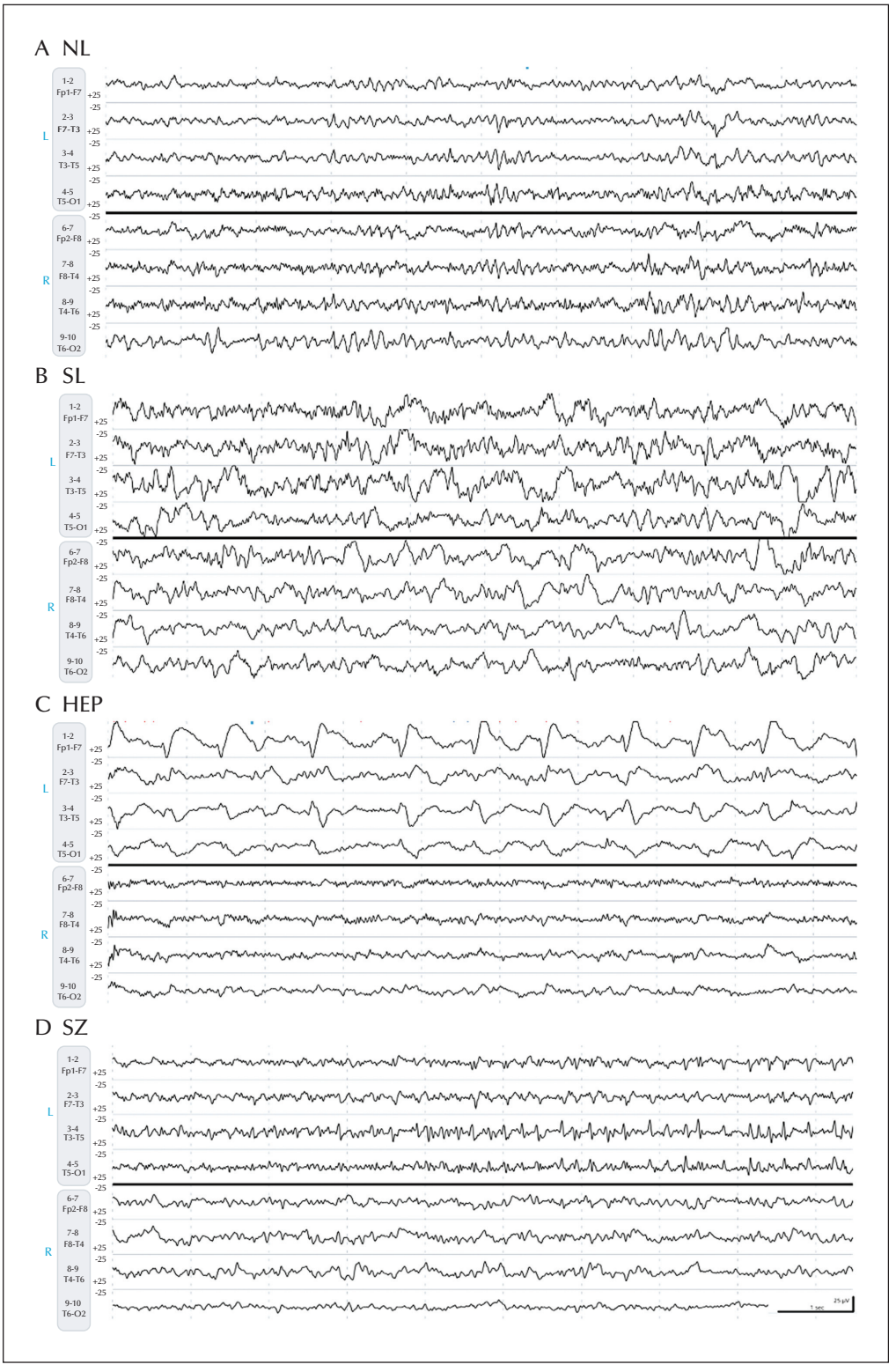
Information on ASMs and sedation and their time of administration before and after rEEG was collected from electronic medical records. ASMs were defined as all FDA-approved drugs for seizures and included benzodiazepines, while sedation agents were defined as propofol or dexmedetomidine. Significance testing to compare the treatment with ASMs between patients with SZ/HEP diagnoses and those with NL/SL diagnosis on rEEG was done using a χ^2 test of independence and a significance level of α=0.05. In cases where long-term video-EEG (LTM-vEEG) recording was present, the EEG report was reviewed, and the date, time, and duration of LTM-vEEG was collected. In cases where rEEG revealed a NL/SL diagnosis but the LTM-vEEG subsequently revealed seizures, we reviewed the clinical course and EEG recordings of these patients.

We selected all the NL/SL rEEG cases in which the subsequent LTM-vEEG recordings in the next 24 hours had captured SZs. To account for interrater variability in interpreting EEG findings and to acquire information about the focality and location of seizures, we asked three independent neurologists (one senior EEG fellow and two attending epileptologists) who were blinded to original rEEG and LTM-vEEG diagnoses to read both rEEG and LTM-vEEG. Each reviewer was asked to note the most prominent electrographic feature present in the EEG recording, and a two-third majority consensus was used as the final interpretation. We also asked the reviewers to note the localization of seizures, and comment if the seizures on LTM-vEEG were only seen in parasagittal/midline regions since rEEG lacks coverage in these regions.

Results

Demographic and clinical characteristics are summarized in *table 1*. Prior to initiation of rEEG, 46% of cases were already treated with ASMs. Across the 100 cases, all rEEG studies were deemed by the reading teams as interpretable. *Table 2* summarizes the electrographic findings in all 100 cases; five patients had non-convulsive seizures (SZ) and 14 had HEPs, while 81 cases had normal or non-epileptic encephalopathic patterns (NL/SL) during rEEG evaluation. As shown in *figure 2*, there was a significant relationship between rEEG findings and escalation of treatment with ASMs or the lack thereof. Overall, cases in which seizures or epileptic abnormalities were ruled out (*i.e.*, NL/SL cases) had significantly less likelihood of being started on or continuing on ASMs (χ^2 = [1, n = 100] = 7.086, p = .0078). Among the 81 NL/SL cases, 30 patients had received sedatives prior to rEEG initiation, of whom 13 were taken off sedation after rEEG. Among the 19 HEP/SZ cases, seven patients were on sedatives prior to rEEG initiation, and only two were taken off sedation following rEEG.

LTM-vEEG was initiated in 54 of 100 cases within 24 hours of rEEG. Comparing the groups with or without LTM-vEEG revealed no significant demographic differences. The median (IQR) duration of rEEG recording was 1.96 (1.00-6.15) hours vs. 27.4 (18.2-54.6) hours for LTM-vEEG. The durations of rEEG and LTM-vEEG recordings were greater in cases with HEP/SZ on rEEG when compared to NL/SL cases (*table 1*).



■ **Figure 1.** A representative sample of electrographic features on rEEG for each of the categories: normal EEG (NL) (A), diffuse/focal slowing (SL) (B), highly epileptiform patterns (HEP) (C), and generalized or focal seizures (SZ) (D).

▼ **Table 1.** Demographics.

Characteristic	All patients
Number of patients	100
Age, in years (median [IQR])	63.5 [47.8 – 63.5]
Female gender, *n* (%)	66 (66%)
Race	
White	50 (50%)
Black or African American	15 (15%)
Asian	11 (11%)
Native Hawaiian or Pacific Islander	2 (2%)
American Indian or Alaskan native	0 (0%)
Other or unspecified	22 (22%)
Ethnicity	
Non-Hispanic, non-Latino, non-Spanish	87 (87%)
Hispanic, Latino, Spanish	13 (13%)
Reason for hospitalization (%)	
Altered mental status	20 (20%)
Cerebrovascular disease	17 (17%)
Fall or found on the ground	7 (7%)
Seizure	11 (11%)
Sepsis	4 (4%)
TBI	4 (4%)
Unilateral weakness	5 (5%)
Other or unspecified	32 (32%)
Duration of rEEG, in hours (median [IQR])	1.96 [1.00-6.15]
NL/SL on rEEG (*n* = 81)	1.85 [0.98-6.08]
HEP/SZ on rEEG (*n* = 19)	3.27 [1.05-5.43]
Duration of LTM-vEEG, in hours (median [IQR])	27.4 [18.2-54.6]
NL/SL on rEEG (*n* = 81)	26.2 [16.3-44.3]
HEP/SZ on rEEG (*n* = 19)	60.4 [29.3-80.8]
Started on ASMs prior to initiation of rEEG	46 (46%)
Started on sedation prior to initiation of rEEG	37 (37%)

rEEG: rapid EEG; LTM-vEEG: long-term video-EEG; NL: normal; SL: diffuse/focal slowing; HEP: highly epileptiform patterns; SZ: generalized or focal seizures.

We studied the relationship between diagnoses made with rEEG compared to LTM-vEEG (*figure 3*). In five patients who had seizures on rEEG, all continued on LTM-vEEG except for one patient with COVID-19 in whom seizures were managed solely on prolonged rEEG recording. In three of the four patients, seizures were effectively treated with ASM before LTM-vEEG, and there were no further seizures detected on LTM-vEEG over the next 24 hours. Only one patient had more seizures on LTM-vEEG monitoring within 24 hours despite being treated with ASMs. Seizure locations and patterns were described as the same on rEEG and LTM-vEEG procedure notes. The seven patients with HEP on rEEG continued without seizures in the next 24 hours of LTM-vEEG, and all remained on ASMs. In four cases, ASMs were initiated before and continued following rEEG, while in the three remaining cases, ASMs were initiated after rEEG.

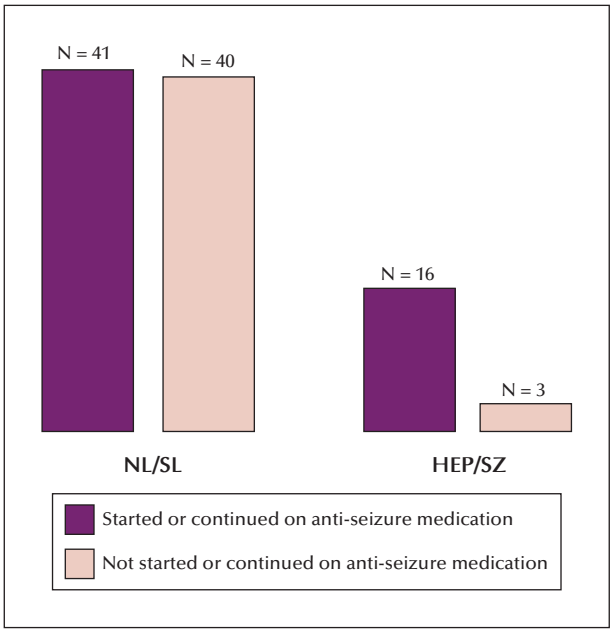
In cases in which LTM-vEEG was acquired following NL/SL patterns on rEEG, six patients were reported to have seizures during the next 24 hours. All of these patients were on ASMs because of the clinical team's high suspicion for possible seizures in these patients. In four patients, ASMs were initiated before and

▼ **Table 2.** Electrographic findings.

Electrographic findings	Number of cases
NL/SL	81
HEP (features could overlap) Abundant sporadic epileptiform discharges Lateralized or generalized periodic discharges Lateralized rhythmic delta activity Bilateral independent periodic discharges	14 10 5 1 1
SZ	5

NL: normal; SL: diffuse/focal slowing; HEP: highly epileptiform patterns; SZ: generalized or focal seizures.

continued following rEEG, while in the two remaining cases, ASMs were initiated after rEEG. The clinical courses of these cases were reviewed in more detail, and three independent neurologists who were blinded to the original diagnoses re-reviewed each rEEG. Our findings revealed the following. In two cases, the independent reviewers classified the rEEG as having abundant epileptiform activity despite the clinical read classifying the rEEG as NL/SL. In two other cases, rEEG was recorded for a short time (<one hour) after patients had received benzodiazepines for witnessed convulsive seizures (one patient had a known history of epilepsy and another patient had a progressive glioblastoma) and clinical suspicion was high for seizures, thus patients were continued on LTM-vEEG. In two cases, seizures were primarily focal and seen only in the parasagittal/midline regions. One of the two patients had diminished voltage in the lateral EEG leads due to a large subdural hematoma, possibly making it difficult to see propagation of parasagittal seizures to lateral temporal leads. The second had active contractions in the leg contralateral to a known stroke, clinically suggesting a parasagittal focus. In none of these cases, seizures were noted in the first hour of LTM-vEEG recordings.

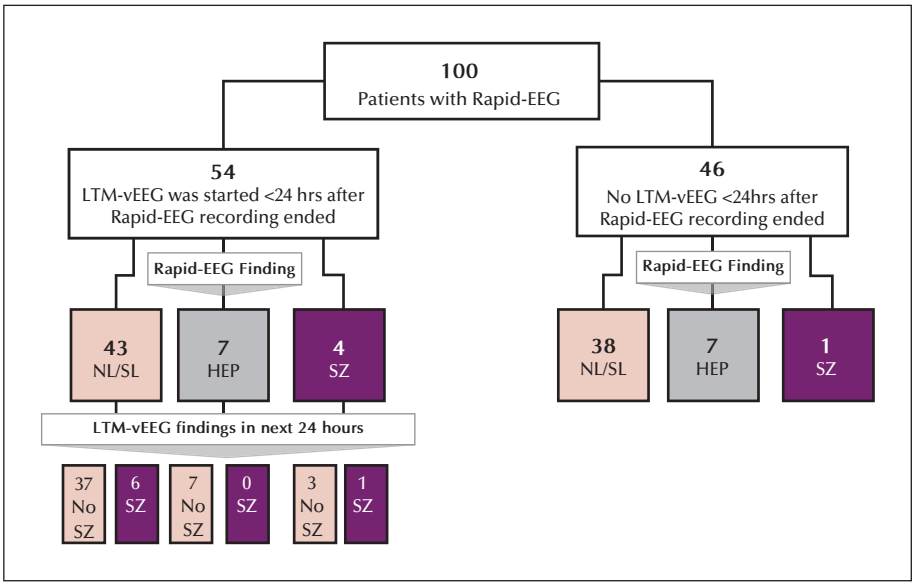


■ **Figure 2.** Relationship between rEEG findings and escalation of treatment with ASMs or the lack of. (NL: normal; SL: diffuse/focal slowing; HEP: highly epileptiform patterns; SZ: generalized or focal seizures).

Discussion

Access to conventional EEG systems may be delayed up to hours at major academic centers [2, 6] and not available at some hospitals. Without access to EEG information, recognition of many cases of non-convulsive status epilepticus may be delayed or missed [7, 8], which in turn may lead to permanent neurological injury [9-13] in these patients. Without EEG information, treatment decisions are often made on the basis of clinical suspicion alone, which may lead to unnecessary overtreatment with ASMs, sedatives, or even intubation [14, 15] before EEG is available. This is supported by our finding that the majority of patients suspected to have seizures do not actually have seizures on EEG, thus ruling out seizures with rEEG may lead to a reduction in the use of anti-seizure treatments in these patients. Our study suggests that the ability to triage patients in a trinary system (NL/SL, HEP, and SZ) can lead to more informed management of patients suspected to have non-convulsive seizures.

Interestingly, recent studies have shown that patients with HEP on early EEG have a higher risk of later seizures within 24 hours of monitoring [14, 15]. However, our findings may suggest that early detection of high-risk patients with rEEG, and their treatment with ASM may reduce the risks of subsequent seizures, as patients with HEP who were treated with ASM did not have seizures in the subsequent 24 hours. We are mindful that this study is limited by its retrospective nature, and that data were collected from a single site that has access to rEEG and epileptologists. Future large-scale prospective studies are needed to confirm the potentially important



■ **Figure 3.** Comparison of diagnoses based on rapid EEG versus LTM-vEEG (long-term video-EEG). (NL: normal; SL: diffuse/focal slowing; HEP: highly epileptiform patterns; SZ: generalized or focal seizures).

findings of this study. Future studies also are needed to determine if early detection of HEP patterns and their treatment with ASM may reduce the risks of subsequent seizures. ■

Key points

- In a review of 100 patients, rapid EEG identified 19 cases with ongoing seizures or highly epileptiform patterns, and 81 cases with neither.
- Ruling out seizures with rapid EEG correlated with a statistically significant reduction in anti-seizure medication treatment.
- Early access to EEG information may lead to more informed and targeted management of patients suspected to have non-convulsive seizures.

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

Acknowledgements and disclosures.
Funding for this research was provided by the Stanford University Medical Scholars Research Program. The authors would like to acknowledge Dr. Aaron Struck (Dept. of Neurology, University of Wisconsin Madison) and Dr. John Stern (Dept. Neurology, University of Los Angeles) for their blinded independent review of EEGs in this study.

The work was not supported by Ceribell and the authors do not have conflicts of interest related to Ceribell. KJM has received research support from the National Institutes of Health and Eisai Pharmaceuticals. The Epilepsy Study Consortium pays Dr. Meador's university for his research consultant time related to Eisai, GW Pharmaceuticals, NeuroPace, Novartis, Supernus, Upsher-Smith Laboratories, UCB Pharma, and Vivus Pharmaceuticals. In addition, Dr. Meador is Co-I and Director of Cognitive Core of the Human Epilepsy Project for the Epilepsy Study Consortium. Dr. Govindarajan is supported by 5R01HS026207 from Agency for Healthcare Research and Quality. Dr. Hirsch is supported by 1R01NS119825. All other authors have no conflicts 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.

Data sharing and availability.
The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, *et al*. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care* 2012; 17: 3-23.

2. Vespa PM, Olson DM, John S, Hobbs KS, Gururangan K, Nie K, *et al*. Evaluating the clinical impact of rapid response electroencephalography: the DECIDE Multicenter Prospective Observational Clinical Study. *Crit Care Med* 2020; 48: 1249-57.

3. Hobbs K, Krishnamohan P, Legault C, Goodman S, Parvizi J, Gururangan K, *et al*. Rapid bedside evaluation of seizures in the ICU by listening to the sound of brainwaves: a prospective observational clinical trial of ceribell's brain stethoscope function. *Neurocrit Care* 2018; 29: 302-12.

4. Yazbeck M, Sra P, Parvizi J. Rapid response electroencephalography for urgent evaluation of patients in community hospital intensive care practice. *J Neurosci Nurs* 2019; 51: 308-12.

5. Leitinger M, Beniczky S, Rohracher A, Gardella E, Kalss G, Qerama E, *et al*. Salzburg consensus criteria for non-convulsive status epilepticus-approach to clinical application. *Epilepsy Behav* 2015; 49: 158-63.

6. Gururangan K, Razavi B, Parvizi J. Utility of electroencephalography: experience from a U.S. tertiary care medical center. *Clin Neurophysiol* 2016; 127: 3335-40.

7. Claassen J, Taccone FS, Horn P, Holtkamp M, Stocchetti N, Oddo M, *et al*. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM. *Intensive Care Med* 2013; 39: 1337-51.

8. 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.

9. Young GB, Jordan KG, Doig GS. An assessment of nonconvulsive seizures in the intensive care unit using continuous EEG monitoring: an investigation of variables associated with mortality. *Neurology* 1996; 47: 83-9.

10. Wagenman KL, Blake TP, Sanchez SM, Schultheis MT, Radcliffe J, Berg RA, *et al*. Electrographic status epilepticus and long-term outcome in critically ill children. *Neurology* 2014; 82: 396-404.

11. Payne ET, Zhao XY, Frndova H, McBain K, Sharma R, Hutchison JS, *et al*. Seizure burden is independently associated with short term outcome in critically ill children. *Brain* 2014; 137: 1429-38.

12. De Marchis GM, Pugin D, Meyers E, Velasquez A, Suwatcharangkoon S, Park S, *et al*. Seizure burden in subarachnoid hemorrhage associated with functional and cognitive outcome. *Neurology* 2016; 86: 253-60.

13. Zafar SF, Rosenthal ES, Jing J, Ge W, Tabaeizadeh M, Aboul Nour H, *et al*. Automated annotation of epileptiform burden and its association with outcomes. *Ann Neuro* 2021; 90: 300-11.

14. Viarasilpa T, Panyavachiraporn N, Osman G, Akioyamen NO, Wasade VS, Barkley G, *et al*. Intubation for psychogenic non-epileptic attacks: frequency, risk factors, and impact on outcome. *Seizure* 2019; 76: 17-21.

15. Uppal P, Cardamone M, Lawson JA. Outcomes of deviation from treatment guidelines in status epilepticus: a systematic review. *Seizure* 2018; 58: 147-53.

TEST YOURSELF

(1) Recent studies have shown that patients with which of the following on EEG have a higher risk of seizures within 24 hours of monitoring?

A. Normal patterns
B. Slowing patterns
C. Highly epileptiform patterns
D. All of the above

(2) Conventional EEG systems are available immediately at all hospitals to evaluate suspicion for non-convulsive seizures. True or false?

A. True
B. False

(3) Which of the following may be consequences of a lack of access to EEG information during the initial neurological evaluation of patients?

A. Missed cases of non-convulsive status epilepticus leading to permanent neurological injury
B. Unnecessary treatment with anti-seizure medications
C. Unnecessary intubation
D. All of the above

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.