



RESEARCH ARTICLE

REVISED The yield of continuous EEG monitoring in the intensive care unit at a tertiary care hospital in Saudi Arabia: A retrospective study [version 3; peer review: 2 approved, 1 approved with reservations]

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Abstract

Background: The practice of continuous EEG monitoring (CEEG) in the intensive care unit (ICU) has spread over the past decade. Building an effective ICU CEEG program demands adequate EEG equipment and human resources. This may not be available in developing healthcare systems. This study sought to shed light on the real-life utility of CEEG at a tertiary healthcare center in the developing healthcare system of Saudi Arabia.

Methods: This is a retrospective review of CEEG findings, along with mortality and duration of hospitalization of patients who had CEEG during a 12-month period at the adult ICU at the King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia.

Results: A total of 202 CEEG records were identified. A total of 52 records showed non-convulsive seizures (NCS); 10 clearly fulfilled criteria for non-convulsive status epilepticus. There were 120 patients that had clinical seizures upon presentation. Among them, 36 (30%) had NCS on EEG. The proportion of patients who were deceased at 60 days was higher in patients with NCS than those who didn't have NCS (42% vs 27%, $\chi^2 = 4.4$, $df=2$, $p=0.03$). There was no statistically significant association between having rhythmic or periodic patterns without NCS and mortality at 60 days or length of hospital stay.

Conclusion: This retrospective study demonstrates a real-world experience from a tertiary care center in Saudi Arabia, a developing healthcare system. ICU CEEG was found to be effective in detecting potentially harmful subclinical patterns, supporting the need to develop ICU CEEG programs. However, the incurred excesses in morbidity and mortality associated with CEEG patterns were relatively modest. Further studies are needed to delineate how the practice of CEEG may be developed in similar healthcare systems to provide meaningful data to clinicians with regards to patient outcomes.

Open Peer Review

Reviewer Status ✓ ✓ ?

	Invited Reviewers		
	1	2	3
REVISED	✓	✓	
version 3		report	
published			
18 Oct 2019	↑	↑	
REVISED	✓	✗	?
version 2		report	report
published			
16 Sep 2019	↑	↑	↑
version 1	✓	✗	?
published	report	report	report
15 May 2019			

- Peter W Kaplan**, Johns Hopkins University School of Medicine, Baltimore, USA
- Robert C. Tasker** , Harvard Medical School, Boston, USA
- Yara Mikhaeil-Demo**, University of Illinois at Chicago, Chicago, USA
Elizabeth E Gerard, Northwestern University (NU), Chicago, USA

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

Neurocritical care, EEG, non-convulsive seizures, status epilepticus, Saudi Arabia

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Author roles: Tayeb HO: Conceptualization, Formal Analysis, Methodology, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

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First published: 15 May 2019, 8:663 (<https://doi.org/10.12688/f1000research.19237.1>)

REVISED Amendments from Version 2

This version of the article provides additional details in the Methods section about the clinical context and the practice setting from which the data have been collected. This includes details of patient selection and case identification. In addition, the author revised the statistical analysis of data concerning rhythmic and periodic CEEG patterns, revealing that having RPPs without non-convulsive seizures was not associated with negative outcomes in this study. Finally, the limitations of this retrospective study of data from a developing ICU CEEG program were better described. [Figure 1](#) was updated for clarification.

Any further responses from the reviewers can be found at the end of the article

Introduction

Continuous electroencephalography (CEEG), the practice of continuously recording an electroencephalogram and a time-synchronized video of the patient, is commonly utilized to monitor critically ill patients with acute brain injury or altered mental status¹. CEEG is instrumental in the diagnosis and management of nonconvulsive seizures (NCS) and status epilepticus, detection of cerebral ischemia, prognostication of outcomes after cardiorespiratory arrest, and evaluation of abnormal movements and altered mental status¹. The practice of CEEG monitoring of critically ill patients in the intensive care unit (ICU) has been spreading in Europe and North America over the past decade^{1,2}. Building an effective ICU CEEG program with sufficient quality demands not only adequate EEG equipment but also significant human resources², including trained electroencephalographers and technologists with enough time to review large amounts of CEEG data². While this is available in large tertiary care centers in North America and Europe where the practice of CEEG has developed, it may not be available in developing healthcare systems with constrained resources.

This study reviewed data generated from a CEEG program in the adult ICU at a tertiary healthcare center in Saudi Arabia, aiming to shed light on the real-life utility of CEEG in a developing healthcare system outside North America and Europe.

Methods

Data gathering

This is a retrospective review of ICU CEEG findings, as well as mortality status and duration of hospitalization of all patients who underwent CEEG monitoring during a 12-month period from September 2016 to August 2017 at the adult ICU at the King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia. This is an academic, tertiary-care, 600-bed hospital. Its adult ICU is comprised of 30 beds and is divided into medical and surgical divisions. The average APACHE II (Acute Physiology and Chronic Health Evaluation II) score of medical patients admitted to the ICU ranges between 10–30 on average. The scores are routinely calculated but not recorded in the electronic medical records (EMR). ICU physicians or neurologists request CEEG to search for NCS or rhythmic or periodic patterns when critically ill patients have a disturbance in the level of consciousness that is unexplained by apparent underlying neurological or medical conditions. Some of these patients also

exhibit paroxysmal motor or non-motor events in association with altered mental status (these are not always consistently recorded in the EMR upon requesting the EEG). During the study period, 120 patients had clinical seizures upon presentation. CEEG is initiated and stopped based on the clinical judgement of the treating physicians. Generally, physicians aim to continue CEEG monitoring for at least 24 hours in patients with altered mental status but may allow discontinuation of CEEG for clinical or practical constraints (e.g. EEG machine availability or the need to relocate a patient to conduct a procedure or test). The electroencephalographer reviews records at least once daily and communicates findings to the treating physicians. If seizures or other CEEG patterns of significance are revealed, physicians often decide to continue or repeat monitoring on subsequent days to guide management. For the purposes of this study, records that continue for several days and those that are within 60 days of each other were considered as one recording. EEGs with a duration that is less than 2 hours were not included in the study as they were considered extended but not long-term studies. An EEG technologist is available during the day time to set up ICU CEEGs. The time from requesting the CEEG to the beginning of the recording varied depending on availability of equipment and technologists. Generally, requests from the ICU are given priority and fulfilled within 24 hours but this is not always feasible. EEG leads are placed using the 10–20 international system of lead placement. CEEGs are digitally recorded, including synchronized video recording of the patient. An epileptologist with fellowship training in CEEG interpretation reviewed the records on daily basis and reported them using the American Clinical Neurophysiology Society (ACNS) ICU EEG consortium proposed nomenclature for ICU EEG reporting, and the Salzburg criteria for non-convulsive status epilepticus³.

Data analysis

Reports of CEEGs performed in the adult ICU during the study period were retrieved from the hospital's EMR. The author extracted key data, including background demographics, diagnoses, length of hospital stay, mortality status at 60 days after admission, and the presence of rhythmic and periodic patterns (RPPs) or NCS. Frequencies, percentages, means, standard deviation, and Chi square were performed using the IBM SPSS Statistics for Windows, version 20.0.

Ethical approval

This study was approved by the Institutional Review Board of KAUH as a retrospective study of anonymized clinical data with waiver of additional patient consent.

Results

A total of 202 CEEG records fulfilling the criteria were identified; complete, raw figures are available as *Underlying data*⁴. There were 116 female patients. The mean age was 53 years (standard deviation=21). The primary diagnosis (as defined by the ICU physicians and entered in the EMR and the EEG requisitions) was epilepsy in 53 patients (26.2%), ischemic stroke in 51 patients (25%), sepsis or metabolic derangement in 40 patients (19.8%), CNS infection in 24 patients (11.9%), intracranial hemorrhage in 10 patients (5%), post-cardiac arrests in 10 patients (5%), brain neoplasm in 8 patients (4%), and traumatic

brain injury in 6 patients (3%). The duration of CEEG recording varied, with 48 (24%) recorded for 2–6 hours and 154 (76%) recorded for longer. **Figure 1** shows a flowchart demonstrating the frequencies of CEEG findings in the sample and their distribution over the outcome categories. There were 52 patients with NCS. Among them, 30 were of focal onset (57.7%) and 10 (5%) clearly fulfilled criteria for non-convulsive status epilepticus. There were 120 patients that had clinical seizures prior to CEEG monitoring. Among them, 36 (30%) had NCS on EEG. A total of 138 records showed RPPs, including 26 that had more than one RPP and 34 of the 52 records with NCS. A total of 78 records had only one type of RPP, including 22 (10.9%) with generalized periodic discharges (GPDs), 20 (9.9%) with lateralized periodic discharges (LPDs), 22 (10.9%) with generalized rhythmic delta activity (GRDA), and 14 (6.9%) with lateralized rhythmic delta activity (LRDA). **Figure 2** shows EEG examples of LPDs and focal and generalized NCS. Sixty two patients (30.7%) out of the entire sample were deceased at 60 days after admission. This proportion was significantly higher in patients who had NCS than those who didn't (42% vs 27%, $\chi^2 = 4.4$, $df=2$, $p=0.03$) (**Table 1**). The frequency of NCS etiologies in the group that was deceased at 60 days is shown in **Figure 1**. There was no statistically significant difference in mortality risk between the etiologies. There was no significant difference in the duration of hospital stay between those who had NCS and those who didn't ($p=0.2$) (**Table 1**). To analyze outcome data in relation to having RPPs, cases with RPPs but without seizures (a total of 104 cases) were considered. There was no

statistically significant difference between the proportion of patients that were deceased at 60 days among those who had RPPs and the same proportion among those without relevant CEEG patterns ($\chi^2 = 0.8$, $df=2$, $p=0.2$). Furthermore, there was no statistically significant difference between the two groups with regards to duration of hospitalization ($\chi^2 = 3.1$, $df=2$, $p=0.2$) (**Table 1**).

Discussion

The practice of using CEEG in the ICU has developed rapidly over the past decade, particularly in North America and Europe^{1,5}. This study is one of the first to report the experience of using ICU CEEG in Saudi Arabia, a country with a rapidly developing healthcare system that faces economic constraints. The data are consistent with prior knowledge and experience from other countries that CEEG is effective in detecting NCS and other likely harmful subclinical EEG patterns^{5,6}. This study reveals statistically significant associations between NCS and mortality, supporting the clinical gestalt of identifying and treating potentially harmful CEEG patterns (although the interpretation of this finding is limited by the inability to control for illness severity and comorbidities in this study). Having RPPs without NCS was not associated with negative outcomes in this study. Furthermore, the potential incurred excess risks of morbidity and mortality in patients with NCS and RPPs was relatively modest. Such modest increases are not likely to be of clinical significance to clinicians evaluating patient prognoses. Nonetheless, this study was a retrospective study with limitations that preclude definitive conclusions about morbidity and mortality risk

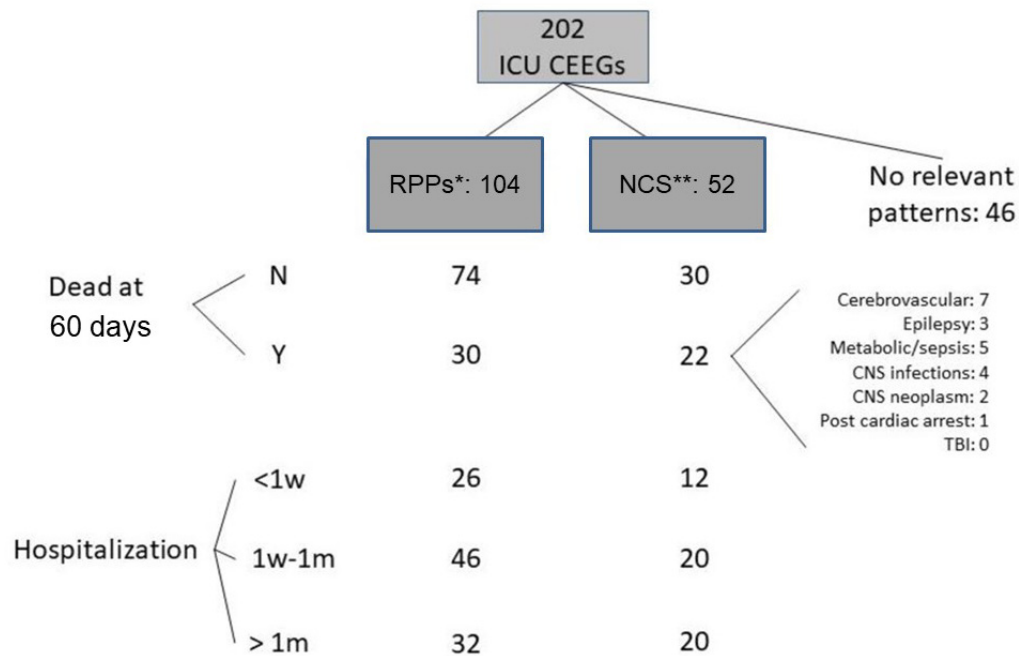


Figure 1. A flow chart showing the frequencies of the CEEG findings, the associated etiologies, and the distribution across outcome categories. * Cases with RPPs without NCS. ** This number includes 34 cases with coexisting RPPs and NCS.

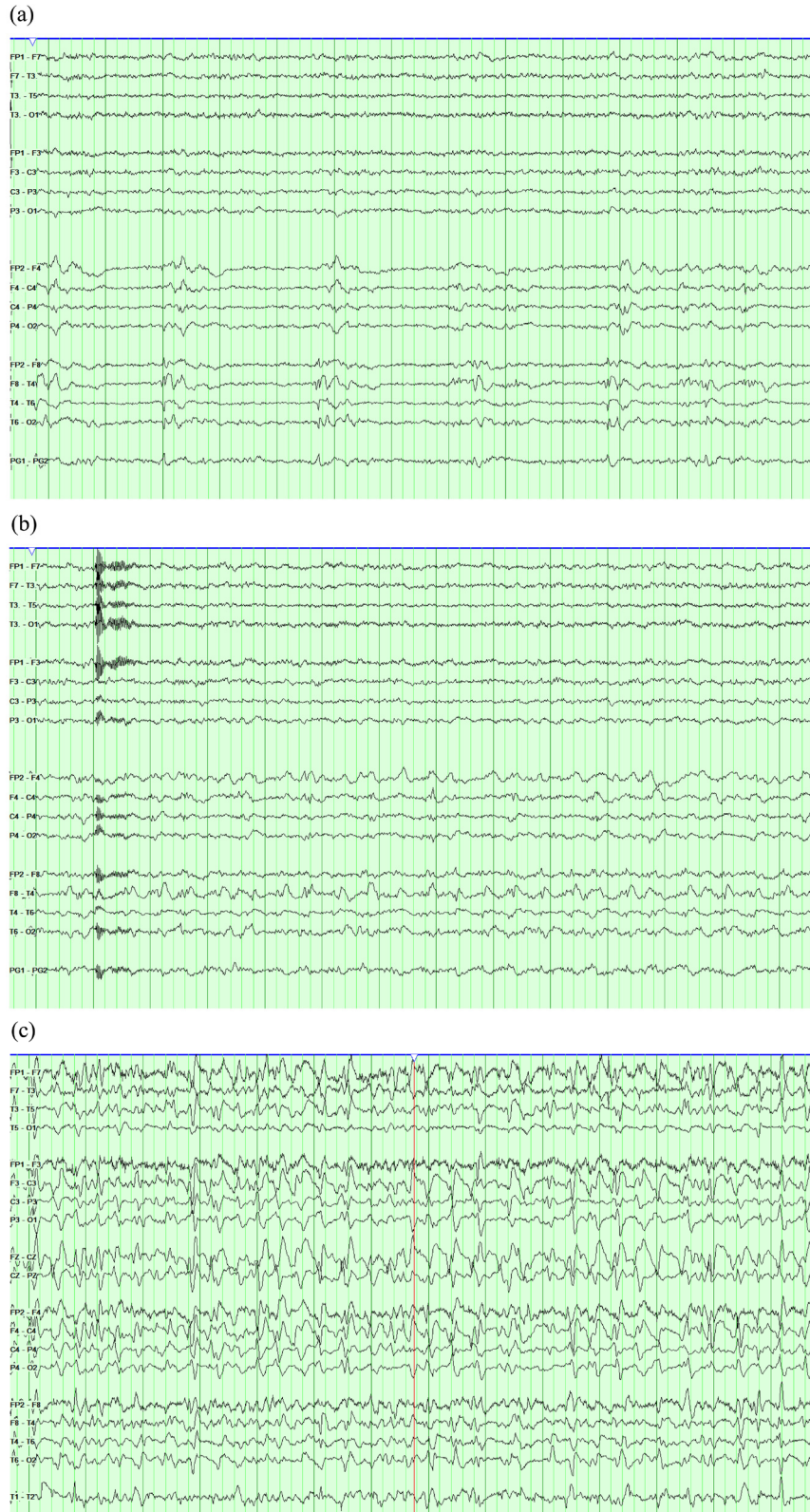


Figure 2. Examples of relevant CEEG patterns from the study sample. EEGs are displayed in a longitudinal bipolar montage with a sensitivity of $7 \mu\text{V}/\text{mm}$ and a time base of 30 mm/second. The high frequency filter is set to 70 Hz and the low frequency filter is set to 1 Hz. **(a)** Right temporal lateralized periodic discharges (LPDs). **(b)** The same record showing evolution of the LPDs into 2.5 Hz rhythmic theta activity, fulfilling seizure criteria. **(c)** Another record showing very long runs of generalized spike and wave activity that recur for most of the recording, fulfilling criteria of non-convulsive status epilepticus.

Table 1. Cross-tabulation of mortality and duration of hospital stay in relation to the presence of non-convulsive seizures (NCS) and rhythmic or periodic patterns (RPPs) on CEEG.

Variable		Mortality		Hospital Stay		
		Dead at 60 days	Alive at 60 days	Hospital stay <1 week	1 week-1month	>1month
NCS	No	40	110	44	62	44
	Row%	26.7%	73.3%	29.3%	41.3%	29.3%
	Col.%	64.5%	78.6%	78.6%	75.6%	68.8%
	Yes	22	30	12	20	20
	Row%	42.3%*	57.7%	23%	38.5%	38.5%
	Col.%	35.5%	21.4%	21.4%	24.4%	31.2%
RPPs	No	10	36	18	16	12
	Row%	21.7%	78.3%	39.1%	34.8%	26.1%
	Col.%	25%	32.7%	40.9%	25.8%	27.3%
	Yes	30	74	26	46	32
	Row%	28.8%	71.2%	25%	44.2%	30.8%*
	Col.%	75%	67.3%	59.1%	74.2%	72.7%

*p<0.05.

magnitudes. These are better assessed by prospective studies and in well-developed CEEG programs.

Prior studies have not definitively proven that utilizing CEEG leads to better outcomes^{2,5}. This, coupled with the significant resources required to effectively run an ICU CEEG program², may lead decision makers in developing healthcare systems to hesitate to support the development of CEEG practices and research. This study presents data from a small and developing program to demonstrate real-world effectiveness of CEEG in detecting potentially harmful electrophysiological patterns. In addition, the study highlights the uncertainties regarding the clinical significance of the prognostic information provided by CEEG. Hopefully, this should lead to further development of ICU CEEG programs with embedded prospective, patient-centered research programs. Such research should focus on how CEEG may be used effectively and optimally and how the generated data may impact clinical decisions and patient outcomes in the ICU.

This study is a retrospective analysis with limitations. Retrospective EMR data did not contain accurate information with regards to the extent and evolution of mental status changes relative to the timing of the CEEG changes, use and titration of sedatives, and other management decisions. Data concerning illness severity were also not recorded in the EMR, limiting the feasibility of controlling for illness severity and comorbidities during the analysis. As such, it cannot be ruled out that differences between groups were in part due to differences in illness severity. It was difficult to ascertain the timing of EEG initiation in relation to these dynamic variables of interest. Physicians did not follow a clear protocol

when deciding the duration of the CEEG study. Furthermore, a selection bias is introduced because of the lack of EEG technologists at night. Shortages in machines and technicians may have affected the duration of CEEG monitoring, as well as treatment decisions and outcomes. Longer studies may lead to higher detection rates of relevant CEEG patterns. Although the total number of cases was 202, the number of cases in most diagnostic categories was not high enough to permit subgroup analyses. The lack of significant associations between negative outcomes and the presence of RPPs without NCS should be interpreted with caution since our data lumped all types of RPPs together and was not sufficiently powered to study each subtype of RPPs. Finally, the clinical setting of this study is that of a developing program with limited resources and must be interpreted in this context. Further studies from developing healthcare systems like Saudi Arabia's are needed to illuminate how the practice of CEEG monitoring may be best utilized to provide clinically meaningful data while caring for patients in the ICU.

Data availability

Open Science Framework: The yield of continuous EEG monitoring in the ICU at a tertiary care hospital in Saudi Arabia: A retrospective study. <https://doi.org/10.17605/OSF.IO/Q56J3>⁴.

This project contains all raw de-identified data associated with this study.

Data are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](https://creativecommons.org/licenses/by/4.0/) (CC0 1.0 Public domain dedication).

References

1. Herman ST, Abend NS, Bleck TP, *et al.*: **Consensus statement on continuous EEG in critically ill adults and children, part I: indications.** *J Clin Neurophysiol.* 2015; **32**(2): 87–95.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
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[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
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[PubMed Abstract](#) | [Publisher Full Text](#)
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<http://www.doi.org/10.17605/OSF.IO/Q56J3>
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[PubMed Abstract](#) | [Publisher Full Text](#)

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Current Peer Review Status:   

Version 3

Reviewer Report 22 October 2019

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Robert C. Tasker 

Department of Neurology, Harvard Medical School, Boston, MA, USA

Thank you - the author has addressed my comments

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pediatric Neurocritical Care; Pediatric ICU

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 18 October 2019

<https://doi.org/10.5256/f1000research.23073.r55420>

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Peter W Kaplan

Department of Neurology, Johns Hopkins Bayview Medical Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 04 October 2019

<https://doi.org/10.5256/f1000research.22446.r54710>

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**Yara Mikhaeil-Demo**

University of Illinois at Chicago, Chicago, USA

Elizabeth E Gerard

Department of Neurology, Feinberg School of Medicine, Northwestern University (NU), Chicago, IL, 60611, USA

This paper describes a one-year experience using continuous EEG monitoring in a developing healthcare system. The authors experience with a growing cEEG program is a valuable addition to the literature. We have some comments and questions to better understand the results described:

Methods:

1. What were the inclusion and exclusion criteria? Was EEG duration less than two hours the only exclusion criteria?
2. How frequently were studies reviewed and results communicated to treating team? It would be helpful to know the timing of when the seizure occurred on EEG and the identification of these findings on EEG and communication with the treating physician.
3. When discussing mortality and morbidity, it would be helpful to adjust for comorbid conditions and severity of underlying illness.
4. In the statistical analysis were p values adjusted for multiple comparisons?

Results:

1. The author indicates a total of 202 cEEG records were identified. Are these for 202 unique patients? Did any patients have more than one cEEG study during this time? If so, were the subsequent studies excluded if the patients had more than one cEEG study during the one year period?
2. How were the clinical diagnoses defined? For example, was “epilepsy” used only if the patient had a prior diagnosis of epilepsy or was it also used for new-onset seizures? Subcategorization of “cerebrovascular disease” would also be helpful. (Based on prior studies intracranial hemorrhage is much more likely to be associated with seizures than ischemic strokes.)
3. In addition to describing the primary diagnosis of the patients it would be helpful to know why they were connected to cEEG. What were the indications for EEG monitoring and frequency for each indication? It would be helpful to describe a table of indication for EEG monitoring and percentage for each reason (example, clinical seizure, altered mental status, abnormal movements, etc).

Discussion:

1. Without adjusting for underlying diagnosis and comorbidities, it is difficult to claim that there is “a significant association between NCS and mortality”.
2. It would be helpful to provide a more detailed discussion as to why the following finding was noted “periodic or rhythmic patterns was significantly associated with longer hospital stays.”
3. In the method section, the author states: “The duration of CEEG monitoring is decided by the neurology consultation or ICU physicians.” It appears that the longest duration for a study was 24 hours; however, as mentioned 52 patients had nonconvulsive seizures, with 10 patients fulfilling the criteria for non-convulsive status epilepticus. How were these patients monitored for response to treatment? Were NCS and NCSE successfully treated by the time of disconnect?
4. Throughout the article the authors refer to the resource requirement for CEEG monitoring. It would be interesting to know if and how resource limitations affected monitoring. What was the time from request to connection? Is there any reason to suspect this affected outcomes?

Figures:

1. Figure 2 is labeled “examples of patterns on the ictal interictal continuum;” however, clear interictal and ictal patterns are shown under this legend.

Tables:

1. Table 1 Title has the words “on cEEG” twice.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 18 Oct 2019

Haythum Tayeb, King Abdulaziz University, Jeddah, Saudi Arabia

Dear Dr. Gerard and Dr. Mickhaeil-Demo,

Thank you so much for taking the time to review the second version of the manuscript and for your valuable comments that have helped me improve it. I have responded to your comments below, point by point.

Methods:

1. What were the inclusion and exclusion criteria? Was EEG duration less than two hours the only exclusion criteria?

Indeed, we included all patients who had CEEG and only excluded cases that did not last for more than 2 hours.

2. How frequently were studies reviewed and results communicated to treating team? It would be helpful to know the timing of when the seizure occurred on EEG and the identification of these findings on EEG and communication with the treating physician.

Thank you for pointing this was not explained. I added this statement in the methods section (line 38 of the manuscript): "The electroencephalographer reviewed records at least once daily and communicated findings to the treating physicians. If seizures or other CEEG patterns of significance are revealed, physicians often decided to continue monitoring on subsequent days to guide management."

3. When discussing mortality and morbidity, it would be helpful to adjust for comorbid conditions and severity of underlying illness.

Thank you for pointing out the importance of controlling for comorbid conditions and illness severity. As stated in the Methods section (line 26 of the manuscript): "The average APACHE II (Acute Physiology and Chronic Health Evaluation II) score of medical patients admitted to the ICU ranges between 10–30 on average. The scores are routinely calculated but not recorded in the electronic medical records (EMR)." As illness severity scores were not recorded in the EMR, the author had no feasible way to control for it during analysis. I added the following statement in the limitations section in the discussion (line 150 of the manuscript): "Data concerning illness severity were also not recorded in the EMR, limiting the feasibility of controlling for illness severity and comorbidities during the analysis. As such, it cannot be ruled out that differences between groups were in part due to differences in illness severity".

4. In the statistical analysis were p values adjusted for multiple comparisons?

The p value was appropriate for the number of comparators and is stated for each analysis.

Results

1. The author indicates a total of 202 cEEG records were identified. Are these for 202 unique patients? Did any patients have more than one cEEG study during this time? If so, were the subsequent studies excluded if the patients had more than one cEEG study during the one year period?

Thank you for pointing this needed to be clarified. I added the following to the Methods section (line 41 of the manuscript): "For the purposes of this study, records that continue for several days and those that are repeated during the same hospitalization or within 60 days of each other were considered as one recording." This was also clarified in the results section (line 74). The outcome of mortality within 60 days and length of hospitalization were defined in relation to the cEEG records defined as such.

2. How were the clinical diagnoses defined? For example, was “epilepsy” used only if the patient had a prior diagnosis of epilepsy or was it also used for new-onset seizures? Subcategorization of “cerebrovascular disease” would also be helpful. (Based on prior studies intracranial hemorrhage is much more likely to be associated with seizures than ischemic strokes.)

The primary clinical diagnosis was defined by physicians taking care of the patient and entered in the EEG requisition. This is now stated results section (line 68 of the manuscript). With regards to the breakdown of cerebrovascular disease, there were 10 cases of intracranial hemorrhage. This is now stated in line 71 of the manuscript.

3. In addition to describing the primary diagnosis of the patients it would be helpful to know why they were connected to cEEG. What were the indications for EEG monitoring and frequency for each indication? It would be helpful to describe a table of indication for EEG monitoring and percentage for each reason (example, clinical seizure, altered mental status, abnormal movements, etc).

All patients had altered mental status. There was no reliable record of associated paroxysmal motor or non-motor events, barring the ability to provide that. This is now stated in line 31-34 of the manuscript.

Discussion:

1. Without adjusting for underlying diagnosis and comorbidities, it is difficult to claim that there is “a significant association between NCS and mortality”.

I now added this statement in the Discussion section (line 129 of the manuscript): ... although the interpretation of this finding is limited by the inability to control for illness severity and comorbidities in this study.

2. It would be helpful to provide a more detailed discussion as to why the following finding was noted “periodic or rhythmic patterns was significantly associated with longer hospital stays.”

Following the advice of another reviewer, the manuscript now presents data of RPPs without NCS, showing no association with hospital stay. The statement in question is now removed and replaced with the following: “Having RPPs without NCS was not associated with negative outcomes in this study” (line 130 of the manuscript).

3. In the method section, the author states: “The duration of CEEG monitoring is decided by the neurology consultation or ICU physicians.” It appears that the longest duration for a study was 24 hours; however, as mentioned 52 patients had nonconvulsive seizures, with 10 patients fulfilling the criteria for non-convulsive status epilepticus. How were these patients monitored for response to treatment? Were NCS and NCSE successfully treated by the time of disconnect?

Thank you for pointing out the need for clarification here. This is now clarified in the methods section as follows: “Generally, physicians aim to continue monitoring for at least 24 hours in patients with altered mental status but may allow discontinuation of CEEG for clinical or practical constraints (e.g. EEG machine availability or the need to relocate a patient to conduct a procedure or test). The electroencephalographer reviewed records at least once daily and communicated findings to the treating physicians. If seizures or other CEEG patterns of significance are revealed, physicians often decided to continue monitoring on subsequent days to guide management. For the purposes of this study, records that continue for several days and those that are repeated during the same hospitalization or within 60 days of each other were considered as one recording.”

4. Throughout the article the authors refer to the resource requirement for CEEG monitoring. It would be interesting to know if and how resource limitations affected monitoring. What was the

time from request to connection? Is there any reason to suspect this affected outcomes?
Thank you for pointing this out. I added this to the Methods section: "The time from requesting the CEEG to the beginning of the recording varied depending on availability of equipment and technologists. Generally, requests from the ICU are given priority and fulfilled within 24 hours but this is not always feasible." I also added this to the limitations section to emphasize this point: "Shortages in machines and technicians may have affected duration of CEEG, treatment decisions and outcomes." (line 158 of the manuscript).

Figures:

1. Figure 2 is labeled "examples of patterns on the ictal interictal continuum;" however, clear interictal and ictal patterns are shown under this legend.

The legend is now changed to "Examples of relevant CEEG patterns from the study sample."

Thank you both very much for your time reviewing this manuscript and making it better.

Sincerely,
Haythum Tayeb

Competing Interests: No competing interests were disclosed.

Reviewer Report 03 October 2019

<https://doi.org/10.5256/f1000research.22446.r53969>

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Robert C. Tasker 

Department of Neurology, Harvard Medical School, Boston, MA, USA

Thank you for the resubmitted report, which I have now read and find much improved. The inclusion of the flow diagram (Figure 1) is a great help. However, some additional points still need to be addressed:

Minor:

1. Page 3, line 4 of Results: please add "years" to the age being quoted.
2. Page 5, line 2 of Figure 2 legend: please change "uV" to the appropriate abbreviation for "microvolts".

Major:

1. I think that Table 1 needs to be corrected. For example, if you consider the top 6 rows related to NCS and check the numbers against the data in Figure 1 there appears to be an inconsistency. For example, row 4 tells us the number of cases with NCS as dead/alive, and by duration <1w/1w-1m/>1m. Cross-checking with Figure 1 the sub-totals for cases with NCS should add-up to 52/202, and of the 52, 22 died and 30 were alive at 60 days (22+30 = 52), which is correct. There is a problem in row 1 (the cases not exhibiting NCS). The total here should be 150 (ie, 202 minus 52). Indeed, for mortality the dead/alive (40 + 110) adds-up to 150. However, in the <1w/1w-1m/>1m

three-way split, the total (44 + 60 + 44) adds-up to 148, and so 2 cases are missing. Please recheck the numbers and percentages, and the statistical tests as described in the text to make sure that everything is correct.

2. Again, Table 1, but now the bottom 6 rows related to RPPs. If you cross-check the numbers against the data in Figure 1 there appears to be some inconsistencies. For example, row 4 (row 10 in the Table) tells us the number of cases with RPPs as dead/alive, and by duration <1w/1w-1m/>1m. Cross-checking with Figure 1 the sub-total of cases with RPP should add-up to 104. however, in the dead/alive split we have $46 + 92 = 138$ (so an extra 34 cases). In the <1w/1w-1m/>1m three-way split, the total ($30 + 62 + 46$) also adds-up 138 (again an extra 34 cases). I think, based on the data in Figure 1, the three-way split (<1w/1w-1m/>1m) should in fact be $26+46+32=104$. Then, the first row of this subsection (row7 in the Table) then needs to be adjusted, and the statistics rechecked.

Thank you for the extra work in doing this - making sure that number are accurate and consistent is always a hard task.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pediatric Neurocritical Care; Pediatric ICU

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 18 Oct 2019

Haythum Tayeb, King Abdulaziz University, Jeddah, Saudi Arabia

Dear Dr. Tasker,

Thank you very much for re-reviewing the manuscript. I highly appreciate the time and effort you invested.

I have made the necessary adjustments you recommended. I added “years” (page 3) and used the appropriate abbreviation for microvolts in the legend for figure 2.

Thank you for pointing out the discrepancy between the table and the flowchart. This discrepancy in the part of the table with data regarding RPPs was because the numbers represented all cases with RPPs (including those who had NCS as well, a total of 138 cases indeed). There was also a typographical error row 1.

Following your recommendation and realizing the importance of separating RPPs from NCS, I made the following changes:

1. I fixed the typographical error in row 1 of the table (60 was changed to 62).
2. I replaced the prior numbers in the last 6 rows of the table with the numbers of cases with RPPs without NCS. When these cases are considered, the association between RPPs and length of hospital stay drops out of significance. Accordingly, I adjusted that in the abstract, results, and discussion sections as well.
3. I changed the flowchart slightly to clarify that that the 52 cases of NCS include cases that also had RPPs.

Once again, thank you for your valuable time, effort, and insights.

Sincerely,
Haythum Tayeb

Competing Interests: No competing interests were disclosed.

Reviewer Report 16 September 2019

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Peter W Kaplan

Department of Neurology, Johns Hopkins Bayview Medical Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: EEG

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 18 September 2019

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Yara Mikhaeil-Demo

University of Illinois at Chicago, Chicago, USA

Elizabeth E Gerard

Department of Neurology, Feinberg School of Medicine, Northwestern University (NU), Chicago, IL, 60611, USA

This paper describes a one-year experience using continuous EEG monitoring in a developing healthcare system. The authors experience with a growing cEEG program is a valuable addition to the literature. We have some comments and questions to better understand the results described:

Methods:

1. What were the inclusions and exclusions criteria? Was EEG duration less than two hours the only exclusion criteria?
2. How frequently were studies reviewed and results communicated to treating team? It would be helpful to know the timing of when the seizure occurred on EEG and the identification of these findings on EEG and communication with the treating physician.

3. When discussing mortality and morbidity, it would be helpful to adjust for comorbid conditions and severity of underlying illness.
4. In the statistical analysis were p values adjusted for multiple comparisons?

Results:

1. The author indicates a total of 202 cEEG records were identified. Are these for 202 unique patients? Did any patients have more than one cEEG study during this time? If so, were the subsequent studies excluded if the patients had more than one cEEG study during the one-year period?
2. How were the clinical diagnoses defined? For example, was “epilepsy” used only if the patient had a prior diagnosis of epilepsy, or was it also used for new-onset seizures? Subcategorization of “cerebrovascular disease” would also be helpful. (Based on prior studies intracranial hemorrhage is much more likely to be associated with seizures than ischemic stroke.)
3. For Table 2, did any patients have more than one of the periodic patterns? Did patients have NCS and periodic patterns? Why is NCSE not listed in the table?
4. It would be interesting to look at the diagnoses associated with NCS, NCSE and periodic patterns.
5. In addition to describing the primary diagnosis of the patients it would be helpful to know why they were connected to cEEG. What were the indications for EEG monitoring and frequency for each indication? It would be helpful to describe a table of indication for EEG monitoring and percentage for each reason (example, clinical seizure, altered mental status, abnormal movements, etc).

Discussion:

1. The author states: “The data are consistent with prior knowledge and experience from other countries that CEEG is effective in detecting NCS and other likely harmful subclinical EEG patterns on the ictal-interictal continuum.” This paper does not define nor discuss the ictal-interictal continuum.
2. The discussion should compare the findings at the current center to prior publications on the yield of CEEG.
3. Without adjusting for underlying diagnosis and comorbidities, it is difficult to claim that there is “a significant association between NCS and mortality.”
4. It would be helpful to provide a more detailed discussion as to why the following finding was noted “periodic or rhythmic patterns was significantly associated with longer hospital stays.”
5. In the method section, the author states: “The duration of CEEG monitoring is decided by the neurology consultation or ICU physicians.” It appears that the longest duration for a study was 24 hours; however, as mentioned 52 patients had nonconvulsive seizures, with 10 patients fulfilling the criteria for non-convulsive status epilepticus. How were these patients monitored for response to treatment? Were NCS and NCSE successfully treated by the time of disconnect?
6. Throughout the article the authors refer to the resource requirement for CEEG monitoring. It would be interesting to know if and how resource limitations affected monitoring. What was the time from request to connection? Is there any reason to suspect this affected outcomes?

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Reviewer Report 23 July 2019

<https://doi.org/10.5256/f1000research.21080.r51103>

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Robert C. Tasker 

Department of Neurology, Harvard Medical School, Boston, MA, USA

The author has described a practice of continuous EEG monitoring in an intensive care unit in a University Hospital in Jeddah, Saudi Arabia.

I have a number of comments that will help readers better understand what these data mean, and how they might reflect on the implications for ICU practice.

Method (page 3)

1. In the first paragraph (line 8) the author describes "CEEG are requested by ICU physician or neurologists according to the clinical needs". In order to understand the significance of some of the analyses provided, it would be helpful to know what were the inclusion criteria, or the 'standard operating procedure' for the ICU. For example, were all patients comatose, and the clinician was unable to assess a clinical response?

2. In the first paragraph (lines 13-15) the authors describes "The duration of CEEG monitoring is decided by the neurology consultation or ICU physicians":
 - In order to understand the significance of some of the analyses later in the manuscript, it would be helpful to know when CEEG was started and finished in relation to admission and discharge/death.
 - It would also be helpful to know the timing of when NCS occurred.
3. Since this population has been gathered from ICU admissions, it would be helpful to have some description of ICU severity-of-illness, according to the risk-adjustment score used by the unit. The examination of any illness feature that might be associated with death needs to be adjusted for severity of illness. There were 62 observed deaths in 200 cases - what was the expected number of deaths from the admission data?

Results (pages 3 and 4)

1. The presentation of findings in the Results section and the Abstract is a little confusing:
 - The author has a starting population of 202 patients undergoing CEEG monitoring. Then, the denominators being used in the data summaries are $n=120$, and $n=200$. I think that a flow chart would help here.
2. Table 2 can be summarized as text, which will make room for a flow-diagram and better review of the data presented in Table 3.
3. Table 3 needs some attention to data accuracy. For example, in Row 2 (Hospital stay data) the percentages add up to 101%, which is just a rounding error. In Row 3 (Hospital stay data) the percentages add up to 99%.
4. Yes, the author has found some associations with death, and length of stay, but does the information gained from CEEG have the potential to help with decision making? For example, if we imagined that CEEG was a 'diagnostic test', then:
 - The pre-CEEG probability of death in this population was 31%. The finding of EEG-seizures could change your pre-test to a post-test probability of death of 39%. I don't think that physicians would find this a helpful piece of information. That is, it is not about death, rather it is something we should use to identify a need for treatment, for example.
 - Similarly, the pre-CEEG probability of hospital stay >1 month was 32%. The finding of periodic or rhythmic patterns could change the pre-test to post-test probability of hospital stay >1 month to 34%. Again, I don't think that physicians would find this a helpful piece of information.
 - Obviously, both of these points would need to be tested and validated in a prospective study (as well as knowing details of when these CEEG features were found), but it may lead to a change in emphasis in the first paragraph of the Discussion.

Discussion (pages 3 and 4)

Based on the above results, one could conclude that identifying EEG seizures on CEEG does not provide a significant 'quantum' in prognostic evidence. Similarly, identifying periodic or rhythmic patterns on CEEG does not provide a significant 'quantum' in identifying cases that will be likely be in-hospital >1 month.

I am wondering whether the focus should be on 'what are we doing the CEEG': surely it is to identify something that we can/should treat; and, to identify something that will help us determine that we no longer need to do CEEG.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

No

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: Researcher in the 'Pediatric Status Epilepticus Research Group' (PSERG);
Journal reviewer; Senior Editor

Reviewer Expertise: Pediatric Neurocritical Care; Pediatric ICU

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 25 Aug 2019

Haythum Tayeb, King Abdulaziz University, Jeddah, Saudi Arabia

Dear Dr. Tasker,

Thank you very much for your time and detailed review of my manuscript entitled: "The yield of continuous EEG monitoring in the intensive care unit at a tertiary care hospital in Saudi Arabia: A retrospective study". I value your insights. I have submitted a new version of this manuscript that took into consideration all of your comments and followed your suggestions as well as the other peer review I received. I respond to your comments below as well:

1. it would be helpful to know what were the inclusion criteria, or the 'standard operating procedure' for the ICU.

I added this statement in the Data Gathering section of the new version of the article to clarify the standard practice of the physicians when it comes to ordering, starting and stopping CEEG: "ICU physicians or neurologists request CEEG to search for NCS or patterns on the ictal-interictal continuum when critically ill patients have a disturbance in the level of consciousness that is unexplained by apparent underlying neurological or medical conditions. CEEG is initiated and stopped based on the clinical judgment of the treating teams. Generally, physicians aim to

continue monitoring for 24 hours in patients with altered mental status but may allow discontinuation of CEEG for clinical or practical constraints (e.g. EEG machine availability or the need to relocate the patients).”

In this developing program, there is no hospital protocol with regards to patient selection, CEEG initiation or termination. This is entirely left to the discretion of the treating physicians and is typically reached through discussion and consultation between neurology and ICU. Generally, all patients with unexplained altered mental status were included. It was difficult to ascertain from the EMR documentation how the mental status evolved during the time of the CEEG, unfortunately. This is a limitation I state in the Discussion section.

2. In order to understand the significance of some of the analyses later in the manuscript, it would be helpful to know when CEEG was started and finished in relation to admission and discharge/death. It would also be helpful to know the timing of when NCS occurred. It was difficult to determine with consistency retrospectively from EMR how the duration of monitoring was decided and when the seizures occurred relative to the outcomes of interest. I agree that this is a limitation and would be best addressed in a prospective study. I added this to the new version of the article in the discussion section: “Retrospective EMR data did not contain accurate information with regards to the extent and evolution of mental status changes relative to the timing of the CEEG, use and titration of sedatives, and other management decisions. It was difficult to ascertain the timing of EEG initiation in relation to these dynamic variables of interest. Physicians did not follow a clear protocol when deciding the duration of the CEEG study.”

3. Since this population has been gathered from ICU admissions, it would be helpful to have some description of ICU severity-of-illness, according to the risk-adjustment score used by the unit. The examination of any illness feature that might be associated with death needs to be adjusted for severity of illness. There were 62 observed deaths in 200 cases - what was the expected number of deaths from the admission data?

Thank you for pointing this out. I added this to the methods section: “The average APACHE II (Acute Physiology and Chronic Health Evaluation II) score of medical patients admitted to the ICU ranges between 10-30 on average. The scores are routinely calculated but not recorded in the electronic medical records (EMR).” This was a limitation of the study and we could not remedy this by calculating scores retrospectively.

4. The author has a starting population of 202 patients undergoing CEEG monitoring. Then, the denominators being used in the data summaries are $n=120$, and $n=200$. I think that a flow chart would help here.

I added a flow chart. Thank you for suggesting it. $n=120$ is the number of patients who had clinical seizures prior to CEEG initiation. This is a group of interest since data have previously shown a ~30% risk of NCS. We replicated this. I removed $n=200$ from the prior reporting of the Chi-square to avoid ambiguity. Thank you.

5. Table 2 can be summarized as text, which will make room for a flow-diagram and better review of the data presented in Table 3.

Done. I expanded table 1 (formerly table 3) by adding row and column percentages.

6. Table 3 needs some attention to data accuracy.

Thank you for pointing this out. I scrutinized the data and ensured accuracy. I fixed several coding errors that altered the proportions slightly without altering the overall outlook of the results as well.

7. Does the information gained from CEEG have the potential to help with decision making?
Thank you very much for highlighting this issue. To address it, I reported the “pre-test” proportions to show that the “post-test” proportions are not of large magnitudes. I also added row and column percentages in table 1.

8. I am wondering whether the focus should be on 'what are we doing the CEEG': surely it is to identify something that we can/should treat; and, to identify something that will help us determine that we no longer need to do CEEG.

Thank you for this insight. I altered the discussion to reflect the uncertainty about the clinical meaningfulness of the prognostic information and highlight the need for prospective studies to address the important questions. This is from the new version of the manuscript: “This study reveals statistically significant associations between NCS and mortality and between RPPs and longer hospital stays, supporting the clinical gestalt of identifying and treating potentially harmful CEEG patterns is worthwhile. However, the incurred excess risks of morbidity and mortality in patients with NCS or RPPs was relatively modest. Such modest increases are not likely to be of clinical significance to clinicians evaluating patient prognoses. Nonetheless, this study was a retrospective study with limitations that preclude definitive conclusions about morbidity and mortality risk magnitudes, which are better assessed with prospective studies and in well-developed CEEG programs.

Prior studies have not definitively proven that utilizing CEEG leads to better outcomes^{2, 5}. This, coupled with the significant resources required to effectively run an ICU CEEG program², may lead decision-makers in developing healthcare systems to hesitate to support the development of CEEG practices and research. This study presents data from a small and developing program to demonstrate the real-world effectiveness of CEEG in detecting potentially harmful electrophysiological patterns. In addition, the study highlights the uncertainties regarding the clinical significance of the prognostic information provided by CEEG. Hopefully, this should lead to further development of ICU CEEG programs with embedded prospective, patient-centered research programs. Such research should focus on how CEEG may be used effectively and optimally and how the generated data may impact clinical decisions and patient outcomes in the ICU.”

Once again, thank you very much for your thorough review of this manuscript and your valuable insights. Much appreciated.

Sincerely,
Haythum Tayeb

Competing Interests: No competing interests were disclosed.

Reviewer Report 23 May 2019

<https://doi.org/10.5256/f1000research.21080.r48822>

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**Peter W Kaplan**

Department of Neurology, Johns Hopkins Bayview Medical Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA

How many of the NCSE were focal versus generalized?

Did not the mortality vary with etiology of NCSE and PDs?

I would add in the final section on limitations of the study that there is perforce selection bias as the EEG techs were not available during certain periods (if I remember, overnight and other times) and this should be stated.

Possibly an EEG example of NCSE should be provided.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: EEG

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 25 Aug 2019

Haythum Tayeb, King Abdulaziz University, Jeddah, Saudi Arabia

Dear Dr. Kaplan,

Thank you very much for kindly reviewing my manuscript entitled: "The yield of continuous EEG monitoring in the intensive care unit at a tertiary care hospital in Saudi Arabia: A retrospective study". I value your insights. I have submitted a new version of this manuscript that took in consideration your comments and followed your suggestions as well as the other peer review I

received. I briefly respond to your comments below as well:

1. How many of the NCSE were focal versus generalized?

I included in the new version of the article that "There were 52 patients with NCS. Among them, 30 were of focal onset (57.7%)".

2. Did not the mortality vary with etiology of NCSE and PDs?

The frequency of NCS etiologies in the group that was deceased at 60 days is now shown in a flow chart figure (figure 1). There was no statistically significant difference in mortality risk between the etiologies. Unfortunately, the number of cases in most subgroups was too small to permit subgroup analysis. I addressed this in the new version of the manuscript.

3. I would add in the final section on limitations of the study that there is perforce selection bias as the EEG techs were not available during certain periods (if I remember, overnight and other times) and this should be stated.

Added.

4. Possibly an EEG example of NCSE should be provided.

Added.

Once again, thank very much for your time and insights.

Sincerely,
Haythum Tayeb

Competing Interests: No competing interests were disclosed.

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