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The diagnostic yield of a 2-h versus a 30-min electroencephalogram for patients with altered mental status in neurological intensive care unit

Nesma Mounir^{1*}, Ehab Shaker Belal¹, Mahmoud Fathi Abozeina¹ and Aliaa Ali Tawfeek²

Abstract

Background The continuous electroencephalogram (cEEG) monitoring is recommended for critical ill patients with altered mental status, The cEEG detects seizure activity and nonconvulsive status epilepticus (NCSE) more efficiently than routine electroencephalogram (rEEG). Yet, cEEG is not widely available in many neurological intensive care units (NICU) in limited resource countries. Ideal study duration, and whether cEEG is useful and cost-effective in terms of patient outcome compared to (rEEG), is still questions under research. The main objective in our study was the relative diagnostic yield of the 2 h, prolonged EEG recording, compared to the 30-min rEEG recording in the NICU.

Results There was no significant diagnostic yield for the 2-h electroencephalogram (EEG) over the 30-min EEG for patient with altered mental status in the NICU. Being with altered mental state in an NICU carries a poor outcome, we found that death occurred in 68.9% of patients. Acute ischemic stroke is the most common cause of altered mental status in NICU by about 53.3% of patients. Less than half of the patients (42.2%) were receiving anti-seizure medications (ASM).

Conclusions As long as the cEEG is not available in the NICU, the 30-min EEG has a good diagnostic yield and it is almost equivalent to the prolonged 2-h EEG, and if the EEG is recommended for a longer duration, we recommend a long-term EEG more than 2 h.

Keywords Routine electroencephalogram (EEG), Altered mental status, Neurological intensive care unit (NICU), Diagnostic yield, Prolonged 2-h EEG

Background

The incidence of seizures in critically ill patients is ranged from 8% to 34% based on continuous electroencephalogram (cEEG) [1] The most common conditions associated with seizure in critical illness include a pre-existing history of epilepsy, direct central nervous system (CNS)

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insults, metabolic derangements, and drug withdrawal or intoxication [2] In critically ill patients with seizures, status epilepticus (SE) must be anticipated [3]. The cEEG detects seizure activity and nonconvulsive status epilepticus (NCSE) more efficiently than routine electroencephalogram (rEEG) [4]. Both European Society of Intensive Care Medicine [2] and American Clinical Neurophysiology Society [5] suggest cEEG for critically ill patients with altered consciousness [5]. There are a lot of unanswered questions related to cEEG monitoring, including the ideal study duration, whether therapy of particular EEG patterns without clinical correlation is necessary, and whether cEEG is useful and cost-effective in terms of patient outcome [6]. Such efforts and costs may be justified if the results of cEEG lead to treatment modifications



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and why not it might improve the outcome [7]. Therefore, on the basis of being in a limited resource, country and the cEEG are not available, yet in our neurological intensive care unit (NICU), the main objective in our study was about the relative diagnostic yield of the 2 h, prolonged EEG recording, compared to the 30-min rEEG recording in the NICU.

Methods

The study is cross-sectional analytic study of 45 consecutive patients, between 16 November 2021 and 25 July 2022, who suffered from altered mental status, whether at the presentation or during the hospital stay, defined as any deviation from the baseline level of consciousness ranged from mild confusion till deep coma, of any age and sex, excluding patients who were on sedation during the 24 h before the EEG recording as it will affect the EEG results. A written informed consent was obtained from patients' first degree relative. The scales used in the clinical assessment of altered mental state are Glasgow coma scale (GCS), Full Outline of Un-Responsiveness score (FOUR score), and Modified Rankin score on discharge (mRS) in patients with ischemic stroke. All the patients underwent a 30-min EEG followed by a 2-h EEG under the same settings (once the EEG was available). All recorded EEGs were evaluated according to the latest standardized American Clinical Neurophysiology Society guidelines (ACNS) for the EEG terminology in the critical care settings, 2021 Version [8], by an expert clinicalneurophysiologist blinded to the clinical data. EEG was recorded digitally using Nicolet vEEG system (Viasys Neurocare ISO 13485) with V32 Amplifier (16 bits digital converter, 32 channel input, bandwidth 0.5-70 Hz, channel crosstalk < 40 dB). 21 scalp electrodes placed according to the international 10-20 system. Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 28. Numerical data were summarized as mean ± standard deviation or median (range), while gualitative data were presented as percentage number (%). Comparisons between EEG ½ and EEG 2 h were done using McNemar test. Probability value (p value) equal to or less than 0.05 is considered significant.

Results

The study included 45 patients, 40% were males and 60% were females. The median age of the participants was 63 years ranging from 19 to 84 years (Table 1). Almost all of the participants (82.8%) were non-smokers. About one-third of the participants were diabetic and hypertensive. Thirteen percent of the participants suffered from metabolic syndrome mostly of renal origin. Previous psychiatric illness and cognitive impairment were present only in a small percentage of cases 6.7% and

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Characteristics	Total number (45)
Age	
Mean±SD	55.8 ± 20
Median (range)	63 (19–84)
Sex	
Male	18 (40%)
Female	27 (60%)
Smoking	
Never smoke	37 (82.3%)
(1–10) cigarettes/day	1 (2.2%)
(11:20) cigarettes/day	4 (8.9%)
(21:39) cigarettes/day	1 (2.2%)
Unknown	2 (4.4%)
Diabetes	
No	30 (66.7%)
Yes, controlled ^a	12 (26.7%)
Yes, Uncontrolled ^a	3 (6.7%)
Hypertension	
No	24 (53.3%)
Yes, controlled ^a	18 (40%)
Yes, Uncontrolled ^a	3 (6.7%)
Metabolic problems	
No	39 (86.7%)
Yes	6 (13.3%)
Type of metabolic problems ($n = 6$)	
Renal	3 (50%)
Hepatic	1 (16.7%)
Hypothyroid	1(16.7%)
Combined	1(16.7%)
Previous strokes	
No	36 (80%)
Yes	9 (20%)
History of Epilepsy	
No	40 (88.9%)
Yes	5 (11.1%)
Epilepsy type ($n = 5$)	
Focal	2 (40%)
Generalized	1 (20%)
Unknown	2 (40%)
History of status epilepticus	
No	41 (91.1%)
Yes, with ICU admission	2 (4.4%)
Yes, without ICU admission	2 (4.4%)

SD standard deviation

^a for diabetic and hypertensive patients, being controlled or not is according to the vitals on admission and the hospital course

13.3%, respectively. While, history of ischemic heart disease was present in about 17.8%; half of them had a history of myocardial infarction (MI) or coronary artery

stenting. Finally, Atrial fibrillation was detected in about 20% of the participants. The most common aetiology among participants was ischemic stroke (53.3%), followed by post ictal state in patients presented by serial fits with altered consciousness (13%), less commonly, CNS inflammatory condition, haemorrhagic stroke, cerebral venous thrombosis, metabolic derangement and neuromuscular respiratory failure (Fig. 1). Glasgow coma scale (GCS) during the EEG revealed that more than two-third of the patients (66.7%) were classified as GCS \geq 8 and the Full Outline of Un-Responsiveness score (FOUR score) showed a median of 13 points (range 0–16). Computerized tomography (CT) brain was done for almost all patients (91.1%). Abnormal CT brain finding was

detected among 80.5% of the patients (Fig. 2). Right and left middle cerebral artery (MCA) with oedema was the most common reported CT brain abnormality (18.2%). Regarding treatment history during the hospital stay less than half of the patients (42.2%) were on anti-seizure medications, mostly combined 52.6%, monotherapy in 47.4% (levetiracetam 36.8%, carbamazepine 5.3%, or phenytoin 5.3%, 15.6% of the patients received specific immune therapy, 93.3% were receiving intravenous antibiotics due to recurrent chest or urinary tract infections. Less than half of the patients (46.7%) were investigated by magnetic resonance imaging (MRI) brain and abnormal finding of MRI was detected in (90.5%) of the participants. The median duration of intensive care unit (ICU)

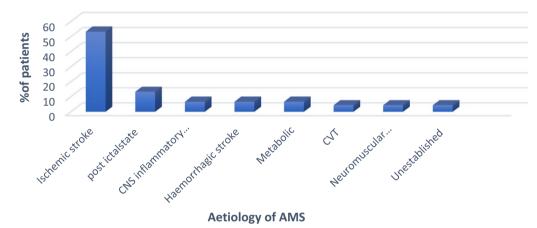


Fig. 1 Aetiology among the participants. CVT cerebral venous thrombosis, CNS central nervous system. AMS altered mental status

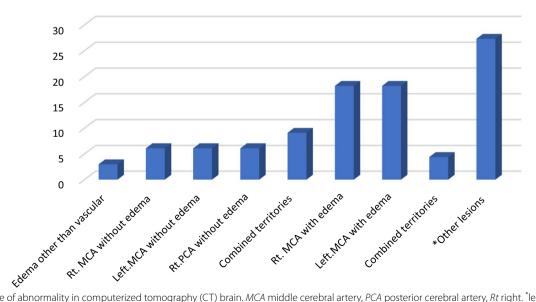


Fig. 2 Type of abnormality in computerized tomography (CT) brain. MCA middle cerebral artery, PCA posterior cerebral artery, Rt right. *lesions that were other than vascular territorial affection

stay was 15 days, ranging from 2 to 70 days. The median duration to obtain an EEG recording for patient with altered mental status (AMS) was 4 days. Regarding modified Rankin score on discharge (mRS), about two-third of the participants 68.9% were dead on discharge. The good outcome (mRS 0:1) was obtained in 8.9% of patients and the rest (about 22.2%) of the patients were discharged with variable degrees of disability. The comparison between the 30-min EEG and the 2-h EEG revealed that, there was no significant difference between the 30-min EEG and 2-h EEG regarding symmetry, posterior dominant alpha with eye closure, voltage EEG and anterior-toposterior (AP) gradient p value (1.000, 1.000, 0.233 and 0.607, respectively) (Table 2). Regarding Predominant background frequency, 30-min EEG detects predominant Beta activity in 11.1% of patients and Delta activity in 6.7%, while 2-h EEG detects Beta activity in 2.2% and Delta activity in 24.4% of patients with statistically significant differences (p value = 0.036) (Fig. 3). The 30-min EEG showed absent state change in 88.9% of patients and state change without stage N2 sleep in 8.9% of the patients, while the 2-h EEG showed absent state change in 66.9% and state change without stage N2 sleep in 26.7%; with statistically significant difference (p value=0.037) in eliciting the state change without stage N2 sleep (Fig. 4). Regarding continuity of the background: during the 30-min EEG, the background was continuous in 95.6% and suppressed in 4.4% of patients, while the 2-h EEG revealed that the background was continuous in 93.3% and suppressed in 2.2%, it also showed a burst attenuation of the background in 2.2% (only 1 patient) and attenuation in 2.2%, Regarding reactivity: it was tested only during the 2-h EEG, we found that our patients were classified as unclear in 22.2%, Reactive in 20%, Unreactive in 20%, and Unknown in 37.8% of the patients. The study did not detect any of the following: sporadic epileptiform discharges (ED), rhythmic and periodic patterns (RPPs), electrographic and electroclinical seizures/status epilepticus, brief potentially ictal rhythmic discharges (BIRDs), ictal interictal continuum (IIC) whether in the 2-h EEG or the 30-min EEG, the majority of EEGs showed variable degrees of generalized slowing.

Discussion

Both European Society of Intensive Care Medicine [2] and American Clinical Neurophysiology Society suggest cEEG for critically ill patients with altered consciousness [5]. However, it may be difficult to apply in centers lacking human and technical resources which explains why such procedure may still be underused. Although its use increased by 10 folds recently but it accounts about 0.3% of the critically ill population EEG recording [9]. The ideal study duration of cEEG is still debatable [10]. In our

Table 2 Comparison between 30-min EEG and 2-h EEG

Characteristics	30-min EEG	2-h EEG	<i>p</i> value
Symmetry			
Mild asymmetrical	1 (2.2%)	1 (2.2%)	
Symmetrical	44 (97.8%)	44 (97.8%)	1.000
Predominant background Frequen	ю		
Beta	5 (11.1%)	1 (2.2%)	
Alpha	3 (6.7%)	3 (6.7%)	
Theta	34 (75.6%)	30 (66.7%)	
Delta	3 (6.7%)	11 (24.4%)	0.036*
Posterior dominant alpha with eye	closure		
Absent	41 (91.1%)	42 (93.3%)	
Present	4 (8.9%)	3 (6.7%)	1.000
Continuity			
Continuous	43 (95.6%)	42 (93.3%)	
Suppression	2 (4.4%)	1 (2.2%)	
Burst attenuation	-	1 (2.2%)	
Attenuation	-	1 (2.2%)	-
Reactivity			
Unclear	-	10 (22.2%)	
Reactive	-	9 (20%)	
Unreactive	-	9 (20%)	
Unknown	-	17 (37.8%)	-
State change			
Absent	40 (88.9%)	30 (66.7%)	
Present with normal stage N2 sleep transients	1 (2.2%)	3 (6.7%)	
Present without stage N2 sleep	4 (8.9%)	12 (26.7%)	0.037*
Cyclic alternating patterns of ence	phalopathy		
Absent	45 (100%)	45 (100%)	-
EEG Voltage			
Normal	39 (86.7%)	37 (82.2%)	
Low	4 (8.9%)	7 (15.6%)	
Suppressed	2 (4.4%)	1 (2.2%)	0.233
AP gradient			
Absent	38 (84.4%)	35 (77.8%)	
Present	7 (15.6%)	10 (22.2%)	0.607
Breach effect			
Absent	45 (100%)	45 (100%)	_

EEG electroencephalogram, AP anterior-posterior

*Significant p value (P < 0.05)

study, the <u>aetiology</u> of AMS was variable; the most common cause was acute ischemic stroke in more than half of our participants (53.3%), followed by post ictal state, accounting for 13.3% of patients, matched with the etiology of critically patients with AMS (a similar population) admitted to a neurology unit [11, 12]. The abnormal CT brain findings were detected in 80.5% of our patients in our NICU and that is close to an 89% abnormality found by Rai and colleagues in a similar population with

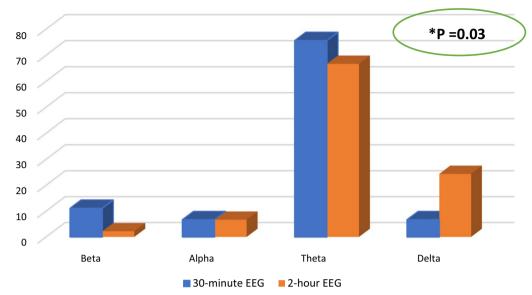


Fig. 3 Comparison between 30-min EEG and 2-h EEG regarding predominant background Frequency. *Significant p value (P < 0.05)

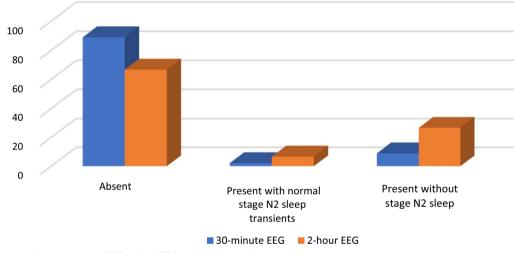


Fig. 4 Comparison between 30-min EEG and 2-h EEG regarding state changes

an AMS [11]. The median duration for the length of stay (LOS) in our NICU, through our population of different aetiologies, was 15 days, ranging from 2 to 70 days, with an in-hospital mortality 68.9%. The good outcome (mRS 0:1) was obtained in 8.9% of patients, and the rest (about 22.2%) of the patients were discharged with variable degrees of disability and it was close enough to the findings of rai and colleagues [11]. The main objective for this work was to find if there is a diagnostic yield for the prolonged 2-h EEG over the routine 30-min EEG, in 45 consecutive patients with altered mental status, and we found that there is no significant diagnostic yield. The majority of our EEGs showed variable degrees of generalized slowing, indicative for a diffuse cerebral dysfunction or diffuse encephalopathy, yet it is a nonspecific feature unrelated to the underlying aetiology [13]. We failed to record any sporadic epileptiform discharges, rhythmic and periodic patterns (RPPs), electrographic and electroclinical seizures/status epilepticus, brief potentially ictal rhythmic discharges (BIRDs), ictal interictal continuum (IIC) whether in the 2-h EEG or the 30-min EEG. Generalized slowing is one of the most common findings in the critical care settings [14], even it might be the most frequent finding [15]. It is considered as one of the nine categories of the baseline EEG pattern according to cEEG monitoring [16] and it is present in half of the requested emergent EEG in the ICU [17]. It should be noted that patient with generalized slowing during the initial EEG recording are unlikely to develop seizure in the subsequent cEEG monitoring [18] and usually carries a better prognosis in comparison with low voltage EEG [13]. Therefore, our EEG findings were different that might be explained by the different methodology; in our study, we did an EEG recording for any patient suffering from AMS (whether at the presentation or during the hospital stay), so we perhaps did an EEG recording for patients who might not be otherwise indicated for EEG, and who might have a clear primary cause for their AMS. These finding were concordant with the study conducted by rai and his coworkers who underwent 1-h EEG versus 72-h EEG, there was no NCSE in any one of the 1-h EEG records and the generalized periodic epileptiform discharges (GPEDs) were seen only in 1% the patients [11]. Another study for patients with AMS in an adult (medical/surgical) ICU who underwent 30-min EEG versus 24 h of continuous video-EEG (cvEEG) monitoring; no epileptiform findings was found during the first 30 min cvEEG monitoring in 66% of patients [10]. In addition, it is still debatable if electrographic seizures, periodic discharge (PD) or NCSE indicate the severity of an underlying disease or whether these abnormalities independently correlate towards an unfavorable patient outcome [7, 19]. Keeping in mind that seizures, independent of the illness severity, are associated with increased morbidity, but not mortality [7]. The current literature suggests that longer duration of EEG recording increases the yield of detecting interictal epileptiform discharges, there is a retrospective study revealed that 2-h EEG has a similar yield as 30-min EEG to detect epileptiform discharges in patients with a normal 30-min rEEG, and it was 3.3% in the 30-min EEG group and 4.2% in the 2-h EEG group. Another study comparing the continuous video-EEG (cvEEG) monitoring and 30-min EEG in an adult (medical/surgical), ICU patient demonstrated that if the cvEEG is not feasible, and a 30-min EEG in the ICU has a high diagnostic yield, providing the majority of epileptiform abnormalities to be detected [10]. In our study, the comparison between the 2-h EEG and the 30-min EEG among patient receiving ASM (42.2% of cases) showed no significant difference. A more recent multicenter study underwent in Switzerland at 4 tertiary hospitals, for critically ill patients with altered consciousness and no recent seizure; cEEG leads to enhanced seizure detection and adjustment of antiseizure medication, but not improved the outcome compared the rEEG. The investigators concluded that in the absence of bigger research, rEEG might be a viable alternative to cEEG in settings with limited resources[18]. In a harmony with our study, this can be applied in NICU settings of limited Page 6 of 7

resources. On the other hand, research was conducted to predict the prognosis of individuals who had altered level of consciousness owing to neurological reasons, found that cEEG (at least 72h) is useful for detecting subclinical seizures, predicting outcomes, and perhaps monitoring the clinical status and responsiveness to therapies such as intravenous antiseizure medication in patients with altered consciousness. This makes cEEG a superior tool for detecting and managing nonconvulsive seizures than single rEEG or serial rEEG recordings [11]. Another more recent research revealed that, the odds of in-hospital death were lower in the cEEG group compared to controls but was not associated with a lower risk of inhospital death. Taking in consideration that, the use of cEEG was linked to a higher median total hospitalization fee and a longer median hospital stay [9] Although the EEG is an important tool for determining prognosis after cardiac arrest, cEEG has no advantage over intermittent rEEG in terms of outcome in cardiac arrest patients and has no effect on the time to death [17]. In our study, there were 7 patients with GCS 3/15 and FOUR score zero at the initiation of EEG recording, analysis of their EEG showed no difference in the diagnostic yield between the 30-min EEG and the 2-h EEG, yet the small number of those patients limited our ability to illustrate such data statistically.

Our research was limited by the unavailability of cEEG monitoring and video EEG monitoring in our NICU, that's why we tried to check whether the prolonged 2-h EEG is more informative than the rEEG and what is the diagnostic relative yield of the prolonged 2-h EEG compared to rEEG. This study, however, may represent a "real-life" clinical practice at several institutions lacking such necessary resources.

Conclusion

There was no significant diagnostic yield for the 2-h EEG over the 30-min EEG for patient with altered mental status in the NICU. Therefore, as long as the cEEG is not available in the NICU, the 30-min EEG has a good diagnostic yield and it is almost equivalent to the prolonged 2-h EEG and if the EEG is recommended for a longer duration, we recommend to ask for a long-term EEG more than 2 h.

Abbreviations

- ACNS American Clinical Neurophysiology Society guidelines
- AMS Altered mental status
- AP Anterior-posterior
- ASM Anti-seizure medication BIRDs Brief potentially ictal rhythmic discharges
- cEEG Continuous electroencephalogram
- CNS Central nervous system
- CT Computed Tomography
- CVT Cerebral venous thrombosis

cvEEG	Continuous video-FEG
ED	Epileptiform discharges
FEG	Electroencephalogram
FOUR	Full Outline of UnResponsiveness
GCS	Glasgow Coma Scale
GPEDs	Generalized periodic epileptiform discharges
ICU	Intensive care unit
IIC	Ictal interictal continuum
LOS	
MCA	The length of stay
	Middle Cerebral artery
MI	Myocardial infarction
MRI	Magnetic resonance imaging
mRS	Modified Rankin score
NCSE	Non-convulsive status epilepticus
NICU	Neurological intensive care unit
p value	Probability-value number
PD	Periodic discharges
PCA	Posterior cerebral artery
rEEG	Routine electroencephalogram
RPPs	Rhythmic and periodic patterns
RT	Right
SE	Status epilepticus
SPSS	Statistical Package for the Social Sciences
%	Percentage number

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Author contributions

NM: data analysis, manuscript writing and reviewing workup, ESB: analyzed research idea, data acquisition, data analysis and interpretation, MFA: performed data acquisition, data analysis and interpretation. AAT: data acquisition and interpretation and manuscript reviewing.

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Availability of data and materials

The data sets generated and/or analyzed during the current study are not publicly available due to the current Cairo University regulations and Egyptian legislation but they are available by a reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the "Research ethical committee (REC) Cairo university Faculty of medicine, Code (MS-612-2021).

Consent for publication

Not applicable.

Competing interests

None of the authors has any conflict of interest.

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