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Chapter

Nonconvulsive Status Epilepticus in Patients with Altered Mental Status Admitted to Hamad General Hospital, Doha, Qatar

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Abstract

This is a prospective, hospital-based study reporting an update and the prevalence of nonconvulsive status epilepticus (NCSE) in patients with altered mental status (AMS) in Qatar. Patients presenting with NCSE are compared to controls. Two-hundred and fifty patients with AMS are involved. Patients with NCSE are: 65 (12–79 years, m, 37, f, 28); controls: 185 (12–80 years, m, 101, f, 84). Occurrence of NCSE in patients with AMS was 26%. NCSE patients were younger than controls ($p < 0.001$). Deaths in the NCSE group occurred in 31% and 19% in controls ($p < 0.0007$). Hospitalization length was longer in NCSE proper and in comatose NCSE compared to controls ($p < 0.02$, $p < 0.03$). Recovery occurred in 40% of NCSE patients and 53% of controls ($p < 0.08$). About 31% of patients ($n = 21$) had refractory NCSE and 9 died. This is the first study reporting the prevalence of NCSE in Qatar. This prevalence (26%) is in the middle range. NCSE did not do better than the controls, result being disappointing regarding comatose NCSE. NCSE is an emerging condition requiring rapid diagnosis and rapid treatment. Regarding the optimal duration of continuous EGG (cEEG) monitoring to diagnose the majority of NCSE cases, 3 days of cEEG monitoring could accomplish this task.

Keywords: nonconvulsive seizures, nonconvulsive status epilepticus, epidemiology, treatment, antiseizure medications, outcome

1. Introduction

Nonconvulsive status epilepticus (NCSE) is accompanied with an altered mental status (AMS) without convulsive motor activity [1]. Because of the paucity of clinical symptoms, EEG is mandatory for the diagnosis of NCSE. In the intensive care unit (ICU), where the patient is often obtunded/comatose, cEEG monitoring is required to reveal NCSE. cEEG monitoring is important because of the difficulty distinguishing when AMS and coma are ictal and differentiating them from non-ictal

Lethargy and confusion attributed to a postictal state
Ictal confusion mistaken for metabolic encephalopathy
Unresponsiveness and catalepsy presumed to be psychogenic
Obtundation thought to be due to alcohol or drug intoxication
Hallucinations and agitation mistaken for psychosis or delirium
Lethargy presumed secondary to hypoglycemia
Mutism attributed to aphasia
Laughing and crying ascribed to emotional lability

Table 1.
Examples of delayed or missed NCSE diagnosis; from Kaplan [48].

symptoms associated with underlying pathology such as posthypoxic, metabolic or septic encephalopathies, and the effects of sedative drugs. Furthermore, the diagnosis of NCSE is frequently delayed, with patients in the ICU having often other serious medical conditions. To diagnose NCSE a high degree of suspicion is required [2], and consequently NCSE remains unrecognized. **Table 1** shows how frequently the diagnosis of NCSE could be missed in the emergency room.

In the United States, the estimated incidence of status epilepticus (SE) is 15–20/100,000 cases per year [3], and NCSE is representing 63% of all SE [4]. Both nonconvulsive seizures (NCS) and NCSE occur very frequently in the ICU and emergency department (ED): NCSs/NCSE is recorded in 8% to 48% in ICU patients [5–8], many of which are fatal [9–11].

Prevalence of NCSE is reported from different geographical areas of the world in patients with AMS [12–16]; However, to our knowledge, there is no study reporting the frequency of NCSE in the Middle East and North Africa (MENA) region; in this vast geographic area, the only NCSE incidence/prevalence is described from the MENA's neighboring countries like Pakistan, India, Turkey, and Israel [17–21]. There is a need for studies regarding the prevalence and morbidity of NCSE in MENA countries [22].

There is also a lack of consensus regarding the EEG monitoring duration when looking for NCSE in ICU patients with AMS; the authors dealing with this issue report a considerable variation in the duration of cEEG monitoring [23–26].

The aims of this chapter are multiple:

a. Know the rate of occurrence of NCSE in patients with AMS admitted to Hamad General Hospital (HGH) Doha, Qatar, using cEEG monitoring.

b. Describe the clinical and EEG findings, causes, head CT/MRI, as well as the treatment and outcomes of NCSE in patients with AMS, and compare the results to a matched control group with similar clinical presentations of AMS.

c. Highlight and discuss the lack of consensus in the literature regarding the duration of cEEG monitoring while looking for NCSs/NCSE in patients with AMS.

2. Methods

This clinical study was performed according to the Good Clinical Practice (GCP) guidelines. Approval was obtained from Hamad Medical Corporation Ethical Committee and Institutional Review Board (IRB). All subjects/relative(s) (caregivers) provided consent before participating.

2.1 Definition of NCSE and AMS

NCSE was defined as an AMS with diminished responsiveness, a positive EEG. and a response to anti-seizure drug (ASD) therapy; as a status, NCSE should be present for a minimum of 30 minutes of continuous nonconvulsive seizure activity or after repeated seizures without recovery of consciousness between events [1]; recently shorter durations have been reported.

Young's criteria [27] of electrographic SE and modified criteria of Chong and Hirsch [28] were used to diagnose NCSE; In addition, the International League against Epilepsy (ILAE) definition and classification of Status Epilepticus [29] and EEG Salzburg Consensus Criteria for NCSE [30] were used to recognize NCSE; NCSE was diagnosed in the presence of continuous generalized spike wave discharges with changes in intensity or frequency, epileptiform activity with ictal patterns that wax and wane, rhythmic and periodic discharges, and subtle and discrete electrographic seizures, when lasting for 30 minutes [10, 13, 15]. In comatose patients, epileptiform discharges faster than 2.5 Hz or generalized periodic discharges (GPDs), lateralized periodic discharges (LPDs) and continuous 2/s GPDs with triphasic morphology [31] of less than 2.5 Hz, as well as rhythmic discharges (RDs) faster than 0.5 Hz were also taken into consideration as NCSE if they responded to benzodiazepine treatment with improvement in the EEG or in patient mental status [13, 15, 29, 32].

Two EEG specialists agreed independently that the patient condition and EEG findings represent NCSE particularly when an EEG pattern did not meet above criteria; finally NCSE was considered if the EEG/or level of consciousness responded to an ASD trial.

Unexplained confusional state, change in behavior, mild to moderate obtundation, alteration in cognition and behavior from baseline, and unexplained decrease in level of consciousness including after convulsive status epilepticus treatment [2, 33] were considered AMS; in elderly patients, delirium (altered level of consciousness, with a fluctuating course, disorganized thinking, and inattention) was also included [15].

2.2 Patient selection for cEEG monitoring

All patients with AMS, from the Emergency Department and from ICUs, aged 12 years or above, had a cEEG monitoring [2, 33]. Not included were patients with open head injury, those whose relatives did not sign the consent form and patients with suspected brain death and an isoelectric EEG. In addition, patients treated for convulsive status epilepticus (CSE) who did not develop later NCSs/NCSE on cEEG monitoring were excluded.

2.3 Patients with NCSE and control group

Patients with AMS and those whose EEG was not compatible with NCSE during 3 days of cEEG monitoring recording were taken as controls. The NCSE and control groups were compared: this included the clinical presentation and medical condition, AMS etiology, neuroimaging, laboratory findings, length of stay, recovery, and outcome

2.4 cEEG monitoring and duration

2.4.1 cEEG recording

The following EEG recording system was used: international 10/20 system with 21 silver/silver chloride cup electrodes. Digital EEG signal stored electronically was filtered for display. High-pass filter and low-pass filter were 0.5–1 and 70 Hz. For

extraneous electrical artifact, 50 Hz notch filter was used; impedance was 100 and 5000 ohms. cEEG was done by EEG technologists and monitored at least twice a day by an EEG specialist.

2.4.2 EEG duration

The duration of cEEG monitoring was determined by the response to treatment of NCSs/NCSE, the presence of other EEG features like rhythmic and periodic discharges, and their responses to treatment.

2.5 Laboratory investigations and Neuroimaging

The following investigations were performed in most NCSE cases and controls: complete blood count, electrolytes, liver and renal functions, brain MRI, and/or CT head; imaging was performed either before or after cEEG monitoring

2.6 NCSs/NCSE treatment

Benzodiazepines (lorazepam or diazepam) were used when NCSs/NCSE was suspected. If seizures persisted, European Federation of Neurological Sciences (EFNS) Guidelines and Glauser et al. report on NCSE treatment were followed: IV diazepam or lorazepam first and then second-line ASDs were initiated—valproic acid, phenytoin, or levetiracetam. If no results, continuous infusions of propofol, midazolam, and barbiturates were used [34, 35].

Many patients received more than one ASD. refractory NCSE was treated with anesthetic agents; same treatment protocol was followed in comatose NCSE. ASDs were not used in control group.

2.7 Outcome parameters

Seizure control and survival/death were considered as primary outcome parameters, while complete recovery and length of stay were secondary outcome parameters.

2.8 Statistical methods

Descriptive statistics (mean with standard deviation) for continuous variables, frequency, and percentages for categorical variables was used; differences between mean levels of NCSE and controls, outcome and morbidity, and Student's t-test were calculated; to detect associations between categorical variables and NCSE vs controls, outcome, and morbidity, chi-square tests or Fisher's exact tests were used. For independent variables at univariate analysis, NCSE logistic regressions were performed using a significance level of 0.05. A P value of 0.05 (two tailed) was considered a statistically significant level. For statistical analysis, an SPSS 22.0 statistical software was used.

3. Results

3.1 Occurrence of NCSE

Six patients suffered from CSE; only one of them who showed later NCSE EEG features and was included in the study. Twenty patients presented NCSs; 30% of them (n = 6) responded to ASDs and did not develop NCSE on cEEG monitoring;

they were also excluded from the study; the rest (70%, n=14) developed later NCSE during cEEG monitoring. These patients were included in the study.

NCSE group: 250 patients with AMS or coma underwent cEEG monitoring. Sixty-two patients were excluded (see reasons above and patient selection). In total, 65 patient responded to the criteria of NCSE (**Table 2**). The occurrence rate of NCSE was 65/250 (26%).

3.2 Characterization of NCSE and the control group

The control group consisted of 185 patients with AMS or coma in which cEEG monitoring did not show any features of NCSE. **Table 2** shows the demographic and clinical features of NCSE and control subjects. Only age and presence of subtle motor phenomena differed between the two groups; the NCSE patients were relatively younger and displayed subtle motor phenomena more often. As for etiology and comorbid states, a history of previous seizures and presence of cortical dysplasia were significantly more common in the NCSE group (**Table 3**). Other etiologies were not informative. Head injury, stroke, and status postcardiac arrest were frequently encountered in accident and emergency patients with NCSE; CT head done in 52

Variable	NCSE (n 65)	Controls (n 185)	P value
Age	45.7 ± 19	52.3 ± 15.8	0.001
Gender	M = 37/F = 28	M = 101/F = 84	0.75
Unresponsive/somnolent	11 (17%)	46 (25%)	0.19
Acute confusion	7 (11%)	18 (10%)	0.81
Severely decreased level of consciousness	20 (31%)	61 (33%)	0.74
Stupor/coma	27 (42%)	60 (32%)	0.23
Subtle motor phenomena	12 (18%)	8 (4%)	0.001

Note: P values are calculated using Chi-square tests and student t tests wherever appropriate.

Table 2.
Characteristics of patients with NCSE and controls.

Variable	NCSE (n 65)	Controls (n 185)	P value
Stroke (hemorrhagic, ischemic, subarachnoid hemorrhage)	16 (25%)	67 (36%)	0.09
Status post cardiac arrest	15 (23%)	35 (19%)	0.59
Head injury	8 (12%)	34 (18%)	0.34
Previous seizures (uncontrolled)	12 (18.4%)	4 (2%)	0.001
Cortical dysplasia	3 (4.6%)	0	0.02
Sepsis	3 (4.6%)	7 (3.8%)	1.00
Hepatic encephalopathy	1 (1.5%)	3 (1.6%)	1.00
End stage renal disease, post renal transplant	2 (3%)	11 (6%)	0.37
Intoxications	0	8 (4.3%)	0.12
Hypertensive encephalopathy	1 (1.5%)	6 (3.2%)	0.68
Personality disorder	1 (1.5%)	3 (1.6%)	1.0
Unknown	3 (4.6%)	7 (3.8%)	1.0

Note: P values are calculated using Chi-square tests or Fisher's exact test wherever appropriate.

Table 3.
Etiology of patients with NCSE and controls.

NCSE cases and in 101 of controls and MRI head done in 41 NCSE cases and in 97 of controls showed hippocampal sclerosis, malformations of cortical development, and encephalomalacia, which were more commonly seen in the NCSE group (**Table 4**).

Abnormal cholesterol and liver enzymes were more often abnormal in the NCSE group than controls (NCSE 15%, controls 4%, p 0.004).

3.3 Length of cEEG monitoring and time of occurrence of NCSs/NCSE

Twenty patients showed NCSs; 65% of them (n = 13) had NCSs during the first 40 minutes of recording, whereas 35% (n = 7) had their seizures later but within the first 48 hours of cEEG monitoring.

In the NCSE group (n = 65), NCSE EEG patterns were recorded during the first 3 hours in 66% (n = 43), later but within the first 48 hours in 22% (n = 14), and in the third day in 12% (n = 8). Among the 22 patients with late NCSE, 17 (77%) were comatose.

3.4 NCSE proper and comatose NCSE

The NCSE group was further subdivided into two: NCSE proper without coma (n = 39) and comatose NCSE (n = 26) [32, 36]; NCSE proper is defined as clinical symptoms suggestive of SE with mild impairment of consciousness (absence status or complex focal SE); NCSE with coma-lateralized epileptiform discharges, NCSE with coma-generalized epileptiform discharges is defined as deep coma of various etiology with characteristic epileptiform EEG pattern but with no clinical motor signs of SE; NCSE proper patients are significantly younger than the comatose NCSE ones (**Table 5**). NCSE in comatose patients was often recorded after the first day of cEEG monitoring: during the first 24 hours in only 54% (n = 14/26), later but within 48 hours in 35% (n = 9/26), and in the third day in 11% (n = 3/26) of the patients; comparatively, NCSE proper was recorded during the first day in 77% (n = 30/39), later but within 48 hours in 10% (n = 4/39), and during the third day in 13% (n = 5/39) of patients.

The 14 patients with early comatose NCSE (first 24 hs) suffered from head injury (n = 4), stroke (n = 4), and cardiac arrest (n = 3); and no etiology was found in three patients; comparatively, in the NCSE proper group (n = 30), 18 patients suffered from previous seizures, 5 from stroke, 3 from sepsis, 2 from head injury, and 2 from cardiac arrest.

Variable	CT (n pts)			MRI (n pts)		
	NCSE (n 52)	Controls (n 101)	P value	NCSE (n 41)	Controls (n 97)	P value
Abnormal	32 (62%)	49 (49%)	0.17	33 (80%)	53 (55%)	0.01
Ischemia, intracerebral hemorrhage, subarachnoid & subdural hemorrhage	14 (27%)	18 (18%)	0.21	16 (39%)	32 (33%)	0.56
Cortical atrophy	5 (10%)	10 (10%)	1.0	3 (7%)	6 (6%)	1.0
Polymicrogyria, cortical dysplasia, heterotopia				3 (7%)	0	0.02
Hippocampal sclerosis	3 (6%)	0	0.04	3 (7%)	1 (1%)	0.08
Encephalomalacia				3 (7%)	10 (10%)	0.04
Meningeal/cortical enhancement	1 (2%)	2 (2%)	1.0	1 (2%)	2 (2%)	1.0

Note: P values are calculated using Chi-square tests or Fisher's exact test wherever appropriate.

Table 4.
Head CT and MRI findings (some patients had both CT and MRI).

3.5 Antiseizure drug (ASD) treatment

Patients with NCSs (n = 20) were treated as follows: 18 with benzodiazepines, 10 with valproate IV, and 8 with levetiracetam plus valproate IV. The 65 NCSE patients received the following: lorazepam 4–8 mg IV or diazepam 10 mg IV (n = 45), levetiracetam IV or PO (n = 22), phenytoin IV (n = 21), valproate IV or PO (n = 18), topiramate PO (n = 5), phenobarbitone IV (n = 7), midazolam IV (n = 15), propofol (n = 5), fentanyl (n = 2), and thiopental (n = 3).

3.6 Outcome

3.6.1 Primary outcome

NCSE group (n = 65): 69% (n = 45, m 25, f 20) responded to treatment within 48 hours, whereas 31% (n = 20, m 12, f 8) died.

Control group (n = 185): 19% (n = 35, m 20, f 15) died. Thus, compared to the control group, death was more frequent in the NCSE group; there was additional statistical significance when NCSE proper was compared to comatose NCSE and when comatose NCSE was compared to controls (**Table 5**), with comatose patients exhibiting a more ominous outcome. The majority of patients with early occurrence of NCSs/NCSE = 65% (40 minutes to 3 hours) died (n = 13/20). Causes of death in NCSE (n = 20) group were distributed as follows: cardiac arrest (n = 6), hemorrhagic and ischemic strokes (n = 5), sepsis (n = 3), head injury (n = 4), subarachnoid hemorrhage (n = 1), and cerebral abscess (n = 1).

3.6.2 Secondary outcome

Compared to controls, NCSE achieved complete recovery in 40% (n = 26, m 15, f 11) compared to controls 53% (n = 98, m 55, f 43); **Table 5** shows that this achieved statistical significance when comatose NCSE was compared to controls; NCSE group (NCSE proper plus comatose NCSE) had a longer hospital stay than the controls.

Variable	NCSE (n 65)	NCSE proper (=without coma) (n 39)	NCSE with coma (n 26)	Control (n 185)	P value
Deaths	20 (31%)	8 (21%)*	12 (46%)*§	35 (19%)§	* 0.05, § 0.0007
Gender male	37 (57%)	23 (59%)	14 (54%)	101 (55%)	
Age (years)	45.7 ± 19§	36.9 ± 24&	51.3 ± 16.9&	52.3 ± 15.8 §	§ 0.001, & 0.006
Hospital stay (days)	15.2 ± 7.7#	14.6 ± 7.8	16.4 ± 7.7^	12.7 ± 5.5#^	# 0.02, ^0.03
Complete recovery	26 (40%)	18 (46%)	8 (31%)a	98 (53%)a	a 0.04

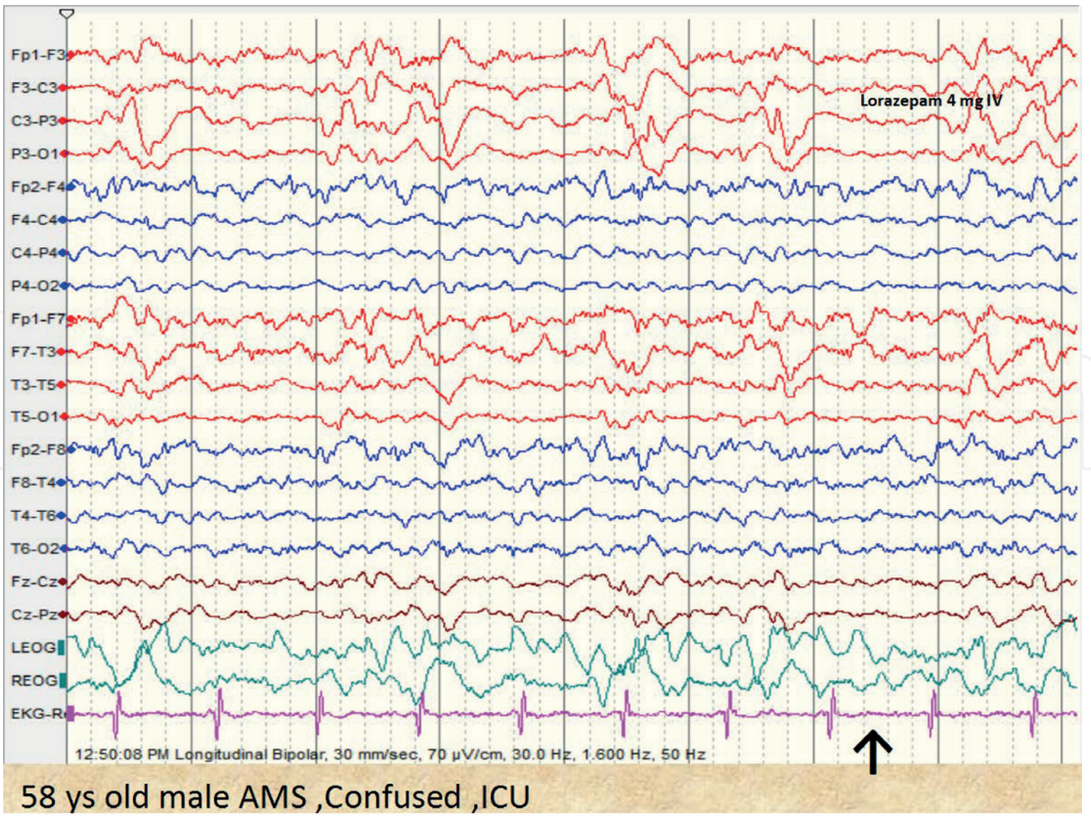
Note: P values are calculated using Chi-square tests, Fisher exact tests and Student t tests wherever appropriate.

** and § compare Death occuring respectively in NCSE without coma to NCSE with coma and also Death occurring in NCSE with coma to controls (respectively 0.05 and 0.0007).*

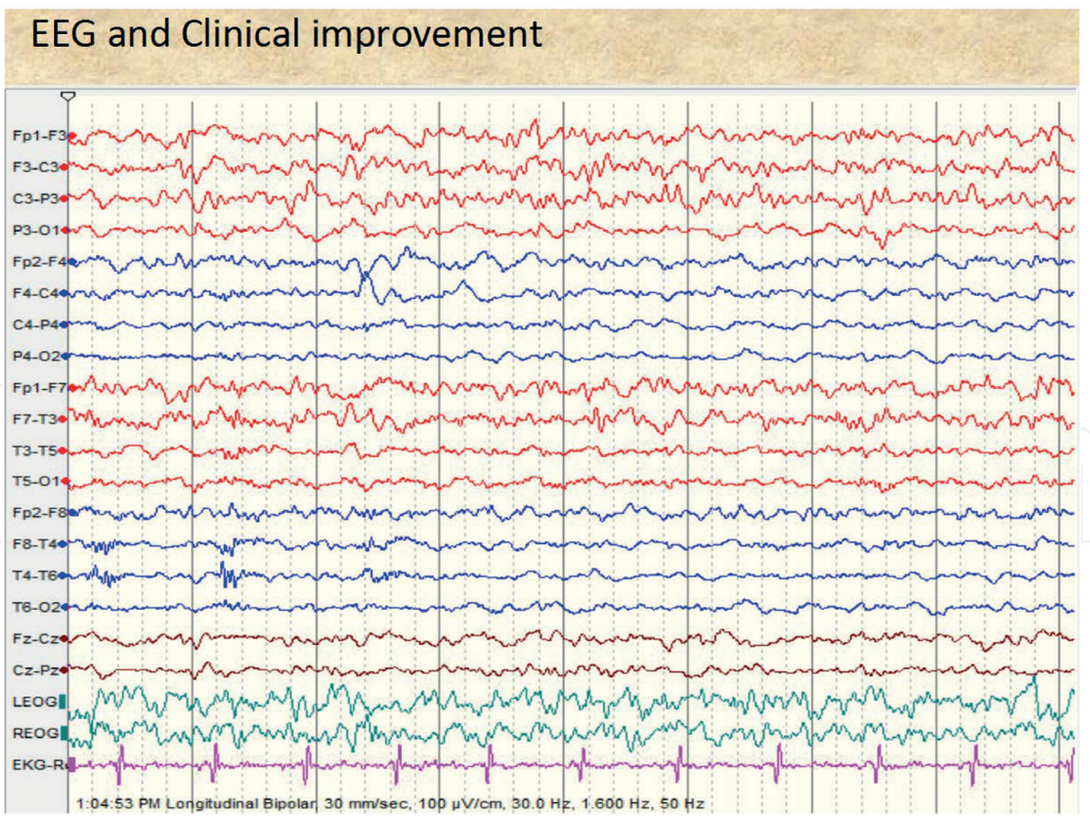
§ and & compare patients and controls 's age respectively in NCSE group to controls and also in NCSE without coma to NCSE with coma (respectively 0.001 and 0.006).

 # and ^ compare hospital stay respectively in NCSE group to controls and also in NCSE with coma to controls (respectively 0.02 and 0.03); symbol a compares complete recovery in NCSE with coma to controls (0.04)

Table 5.
Occurrence and comparison of the listed variables in the NCSE groups and control group.



(a)



(b)

Figure 1.
(a) EEG shows left LPDs; patient received 4mg lorazepam IV and (b) EEG and clinical improvement following lorazepam IV.

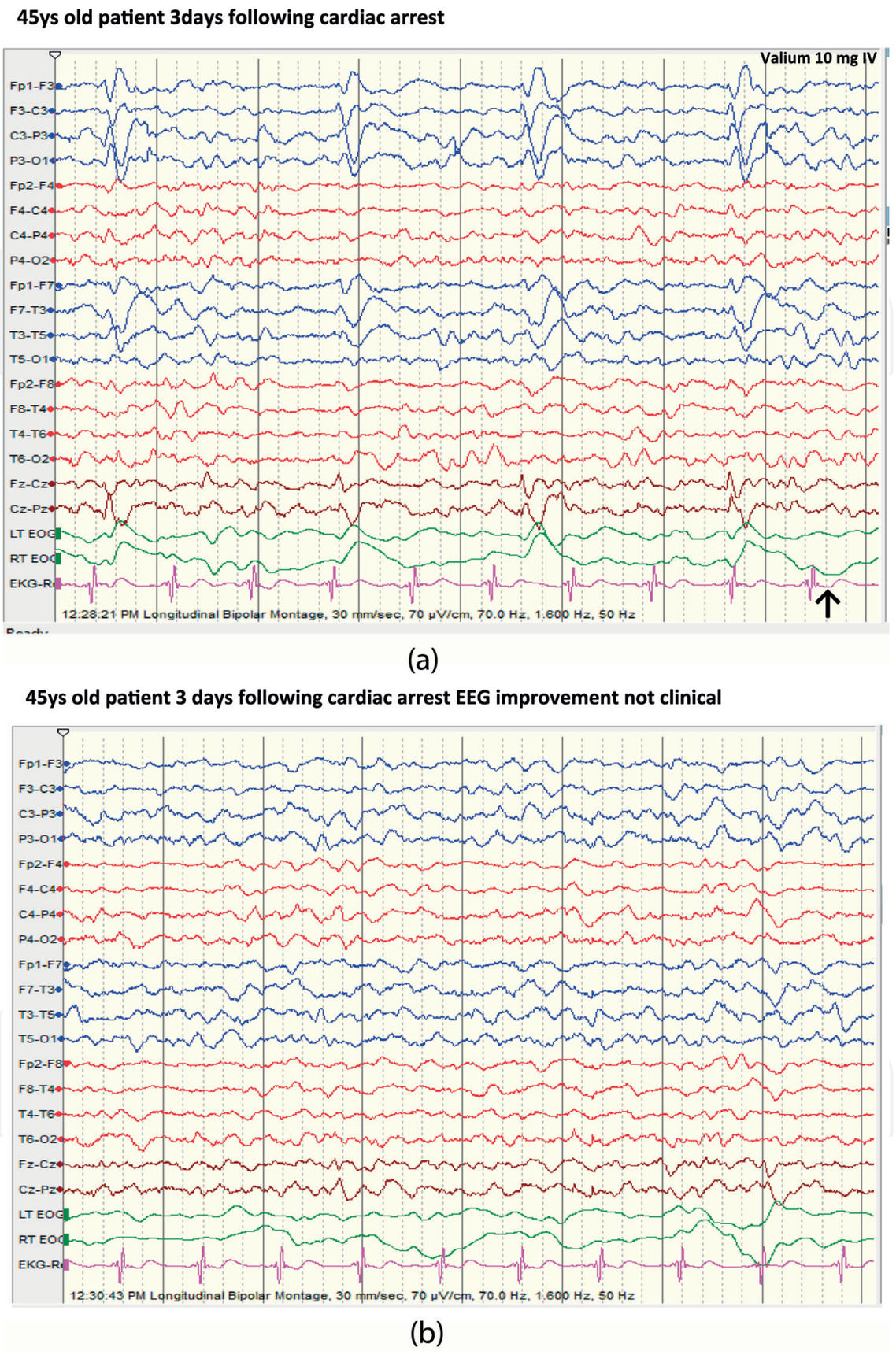
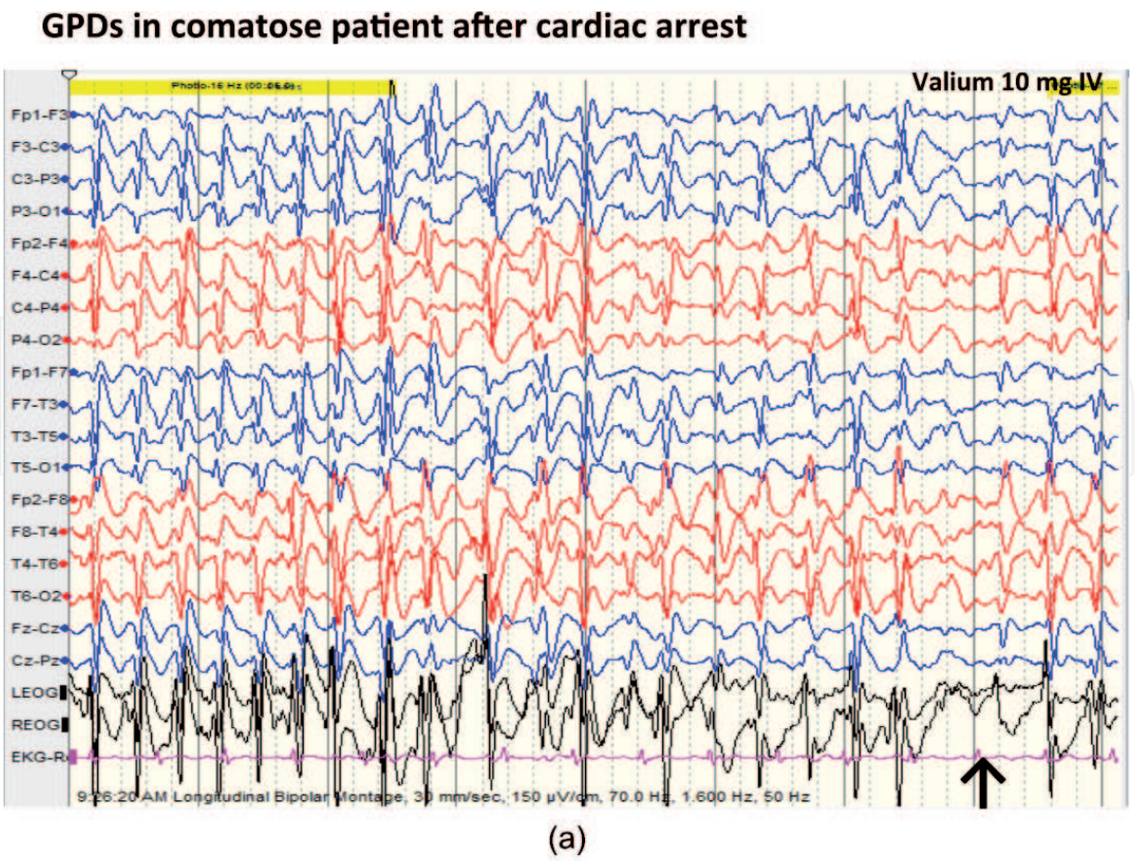


Figure 2.
(a) EEG shows left LPDs in a comatose patient following cardiac arrest; patient receives 10 mg Diazepam IV and (b) EEG shows dramatic improvement following Diazepam IV; however the patient remains comatose (possible NCSE ?).



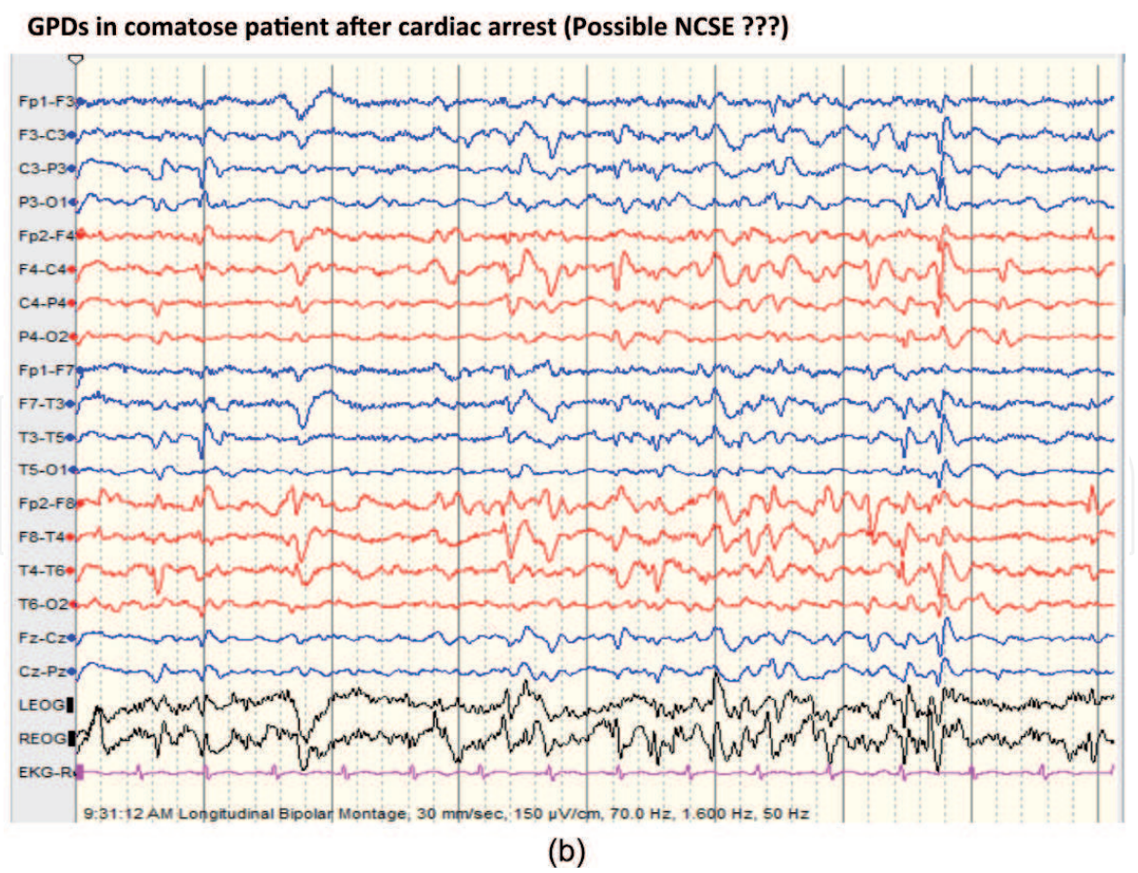


Figure 3.
(a) EEG shows evolving GPDs with triphasic morphology and (b) EEG demonstrates some improvement following Diazepam; however the patient remained comatose.

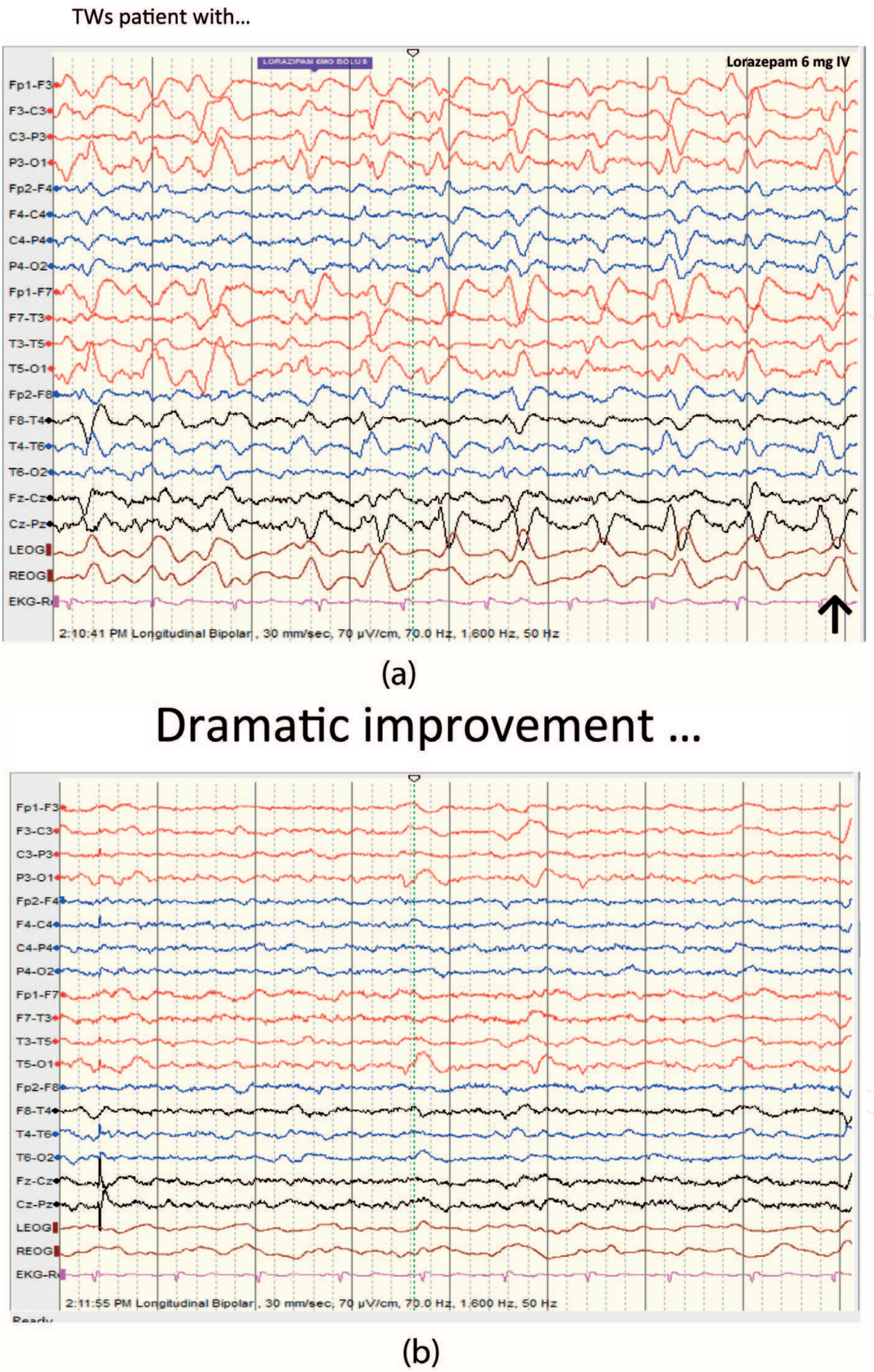


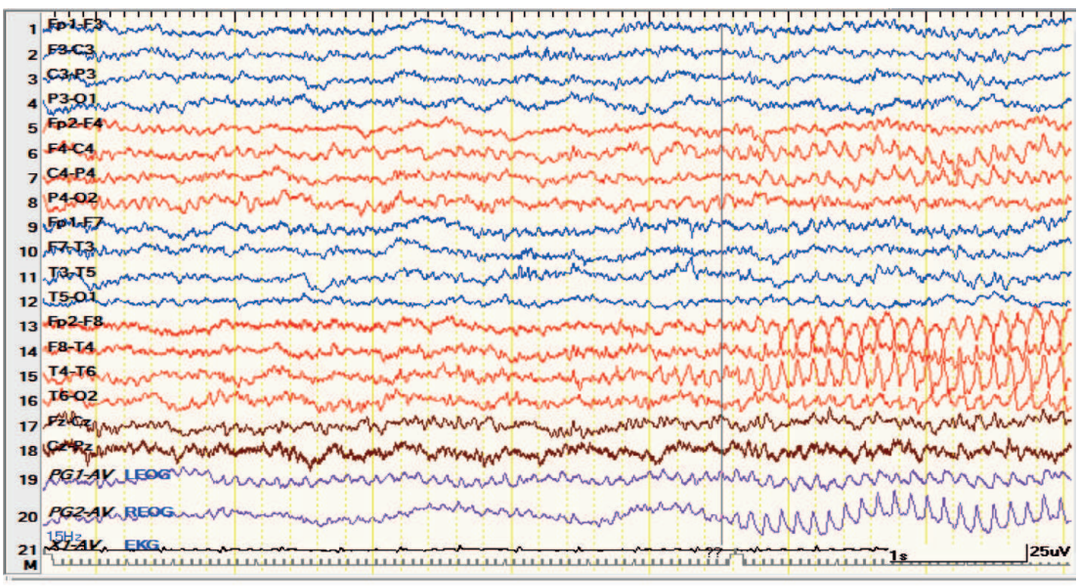
Figure 4.
(a) EEG shows predominantly left sided LPDs with triphasic morphology; 32 years old male given baclofen 30 mg for spasticity the first day of admission; 2 days later he presented an altered mental status with "akinetic mutism"; patient was given 6 mg lorazepam IV bolus. (b) Dramatic improvement in EEG and clinical status following IV lorazepam ; patient recovered completely, started talking and moving around normally; he was found to have a moderate to severe renal impairment (responsible for baclofen intoxication ?).

3.7 Refractory NCSE

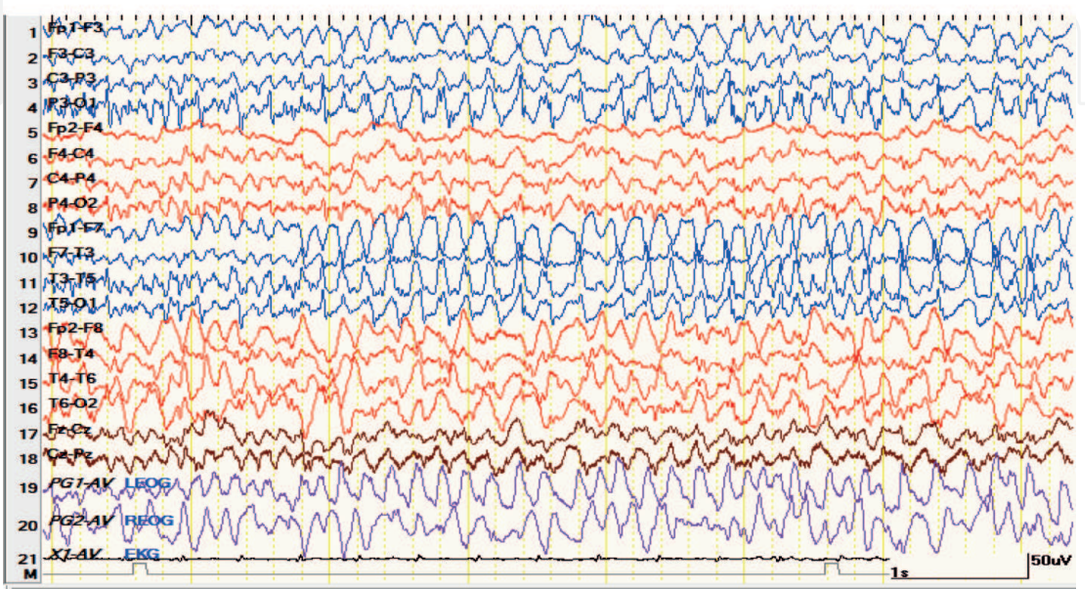
Thirty-two percent of patients with NCSE (n = 21, m 13, f 8) suffered from refractory NCSE, defined as seizures lasting more than 60 minutes with failure of two ASDs [37]; they received the following treatment: midazolam IV (n = 10), propofol (n = 5), thiopental (n = 4), and fentanyl (n = 2). Fifty-seven percent (n = 12, m 8, f 4) survived; forty-three percent (n = 9, m 5, f 4) died with the following reasons: cardiac arrest (3), sepsis (3), ischemia (1), subarachnoid hemorrhage (1), and cerebral abscess (1). Only 33% (n = 7, m 4, f 3) recovered completely.

3.8 EEG patterns and location

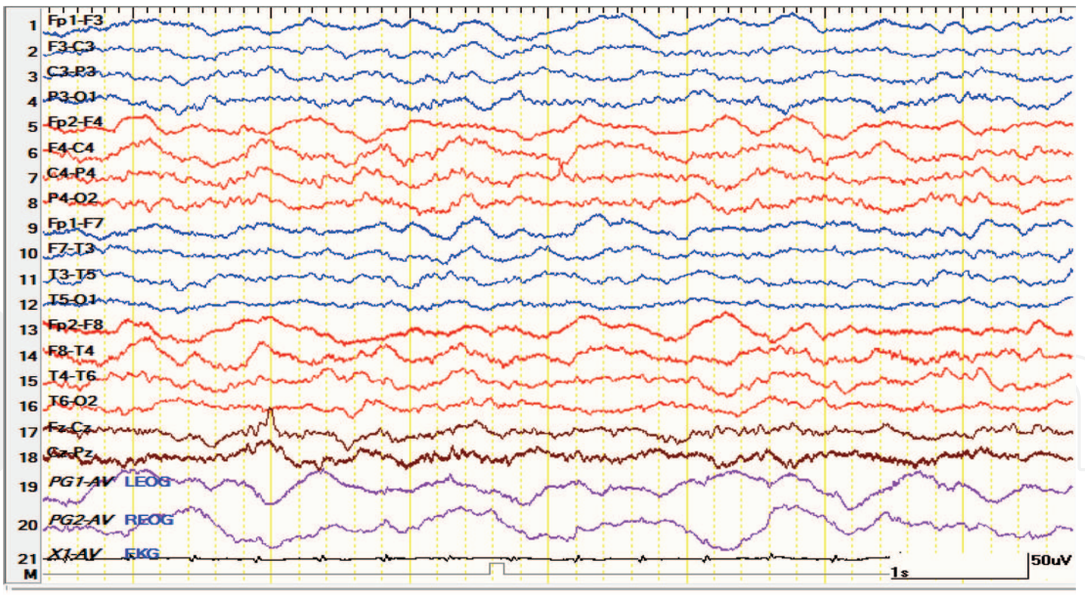
EEG patterns recorded in the NCSE patients (n = 65): focal spike/sharp and wave >3/s in 43% (n = 28), generalized spike/sharp and wave >3/s in 28% (n = 18), GDPs, LPDs, continuous 2/s GPDs with triphasic morphology in 25% (n = 16), and multifocal spikes in 4% (n = 3); **Figures 1–5** show NCSE EEGs cases before and after ASD treatment.



(a)



(b)



(c)

Figure 5.
(a) (Comatose focal NCSE) 67 years old male comatose, following head injury. EEG shows abnormal fast activity starting in right fronto-temporal leads accompanied by abnormal eye movements and facial twitching. (b) The ictal fast activity spreads to the contralateral fronto-temporal leads; patient shows same clinical manifestations (discrete twitching of the left face); the abnormal electrical activity was continuous for more than 30 mn. (c) 1 minute following 2 mg of lorazepam IV; patient remains comatose; EEG shows diffuse generalized slowing; no epileptiform activity; no clinical manifestations; survived with memory impairment and left hemiplegia.

EEG in NCSE patients who ultimately died (n = 20): 40% periodic patterns (n = 8), 30% continuous generalized spike/sharp and waves (n = 6), and 30% with focal spike/sharp and waves (n = 6). Fifty-two percent (n = 34) showed a continuous ictal pattern, and forty-three percent (n = 28) an intermittent/recurrent ictal pattern; five percent (n = 3) were not classified; forty-six percent (n = 30) showed a focal onset and 29% (n = 19) a generalized onset; twenty-five percent (n = 16) showed a periodic pattern; focal seizures originated from the temporal areas (55%) and from the frontal areas (31%). In the control group (n = 185), focal/generalized slowing was seen in 43% (n = 80) and slowing with some spike/sharp wave activity in 2% (n = 4).

4. Discussion

4.1 NCSE prevalence

In the current longitudinal prospective hospital-based study, we investigated the frequency of NCSE in patients with AMS admitted to Hamad Hospital, Doha, Qatar. The prevalence of NCSE among patients with AMS was 26% at our center that is compatible with previous similar studies (prevalence = 16–37%) (**Table 6**); these researchers used a similar design, with a parallel control group; however, most were retrospective, the cEEG recording duration often shorter or not mentioned. Five other authors from MENA' s neighboring countries (mentioned in Section 1) also reported the prevalence of NCSE in patients with AMS; however, they used different study designs, and therefore, those studies cannot be compared with our study.

4.2 NCSE outcome

NCSE is often associated with a poor outcome and a high mortality rate [9, 12, 13, 38]. In the current study, the mortality rate among patients with AMS and

Author (year)	Methods	Duration of EEG recording	Patients with AMS (n)	Patients with NCSE (n) (%)	Outcome
Mesraoua et al. (2017) Current study	Prospective	72 hs	(250)	65 (26)	Response to ASDs: NCSE 45/65 (69%); death: NCSE 20/65 (31%); death in controls: 35/185 (19%); complete recovery: NCSE 26/65 (40%); controls 98/185 (53%); NCSE longer hospital stay than controls $p < 0.02$ (**Table 5**)
Laccheo et al. [38] (2015)	Prospective	>24hs	(170)	36 (21)	Mortality 31% NCSE vs 14% in controls
Kurtz et al. [12] (2014)	Retrospective	?	(154)	NCSE/NCSs 24 (16), PEDs 45(29)	NCSs/NCSE independently associated with poor outcome 20% vs 3% controls, $p = 0.039$
Bottaro et al. [13] (2007)	Retrospective	20mn	(124)	22 (18)	NCSE significant association with mortality, longer hospitalization and poor outcome
Privitera et al. [9] (1994)	Prospective	30mn	(198)	74 (37)	Death was more common in NCSE (37%) compared to controls (23%)

Table 6.
Current and previous studies on NCSE prevalence and outcome.

Variable	OR	95% CI	P value
Age	1.16	1.0–1.34	0.05
Length of stay	2.03	1.29–3.20	0.002
Cardiac arrest	3.27	0.07–153	0.55
Stroke	35.0	0.33–3629	0.14
Head injury	30.1	0.02–56,392	0.38

Note: Variables significant at univariate analysis and having adequate numbers were used for multivariate analysis.

Table 7.
Multivariate logistic regression for mortality in NSCE.

NCSE was 31%, while the mortality rate among those with AMS and without NCSE was only 19%; NCSE carried a poor prognosis. Only one author reported similar outcome in NCSE and controls [9]; however death was more common in NCSE (37%) than in controls (23%). As previously reported by Young et al. [27], the length of stay and age were statistically significantly associated with mortality in the NCSE group (**Table 7**). In addition, in the current study, among patients with AMS and NCSE, head injury and stroke were associated with bad clinical outcomes with regard to recovery (**Table 8**). Also, we observed a longer hospitalization for NCSE group than that in the controls that is compatible with previous reports [13, 15].

We agree with Claassen [14] that most patients showing early NCSE EEG features (n = 13, =65%) did not achieve good outcome; we did not find any association between acute symptomatology and outcome as highlighted by Kang [39].

Patients with "periodic discharges" did not completely meet the EEG criteria for NCSE. In ICUs and cEEG monitoring units, these periodic EEG patterns are described as lying along an ictal–interictal continuum. There are convincing studies that these PDs, especially GPDs and LPDs, are strongly associated with NCSE and may be ictal [13, 15, 32, 40–45]; in fact, these EEG patterns have been found in patients with AMS,

Variable	OR	95% C.I.	P value
Age	1.0	0.96–1.05	0.74
Length of stay	1.10	0.90–1.34	0.36
Cardiac arrest	4.22	0.64–27.9	0.14
Stroke	26.30	3.24–213	0.03
Head injury	19.5	1.30–293	0.002

Note: Variables significant at univariate analysis and having adequate numbers were used for multivariate analysis.

Table 8.
Multivariate logistic regression for morbidity in NSCE.

some were evolving and some responded to benzodiazepines, as shown in **Figures 1–4**. Many studies reported that PDs carry a bad prognosis, and the final outcome depends mainly on the etiology of AMS [8, 18–20, 39]; in our study, 50% of patients with PDs died; they suffered from stroke, cardiac arrest, sepsis, or head injury. However, in multivariate logistic regression analysis, we did not find a correlation between these etiologies and mortality in patients with AMS and NCSE (**Table 7**). It seems that prognosis in NCSE depends on several factors (e.g., age, etiology, level of consciousness, etc.) and cannot be based on EEG or any one factor alone [20, 42].

Finally, the outcome of refractory NCSE was very poor in our study; 9 out of 21 patients (43%) with refractory NCSE died; this is much higher than that reported in a previous study (25%) [46]. However, in that study, 17% of refractory NCSE patients were in a vegetative state.

As reported previously, history of epilepsy/seizures could be a risk factor for NCSs/NCSE [12, 13, 38].

4.3 cEEG monitoring duration

The optimal length of cEEG monitoring in critically ill ICU patients with AMS is a controversial issue in the literature. In our study, majority (66%) of NCSE cases were detected during the first 3 hours of cEEG monitoring; this detection rate reached to 90% by 48 hours of monitoring. Various required cEEG monitoring durations have been suggested in the literature; 12–24 hours [8, 12, 19, 22], 72 hours [16, 18, 47], and finally 7–10 days [23]. A recent study reported that 1/5 of patients without early EEG epileptiform features develop them during 72 hours of cEEG monitoring [25]; Claassen et al. concluded that seizures are detected only in 87% of comatose patients compared to non-comatose patients (98%) in the first 48 hours of cEEG monitoring [14].

Based on the results from our study and review of the literature, and also considering the challenges and costs associated with cEEG monitoring, we suggest that 3 days of cEEG monitoring is optimal in ICUs and in patients with AMS to detect the majority of cases of NCSs/NCSE [14, 25].

5. Conclusion

To our knowledge, this is the first prospective study reporting the prevalence of NCSE in Qatar, a small country in the MENA region. This figure (26%) was in the middle range. Patients with NCSE did not do better than the controls, the result being disappointing regarding comatose NCSE. NCSE is an emerging condition requiring rapid diagnosis and rapid treatment. Regarding the duration of cEGG monitoring to diagnose the majority of NCSE cases, 3 days of cEEG monitoring could accomplish this task.

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