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Clinical profile and comparison of scoring tools for the prediction of in-hospital mortality in convulsive status epilepticus in elderly☆

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ABSTRACT

Purpose: The present study was aimed to study the clinical profile, etiologies, and outcome of convulsive status epilepticus (CSE) in elderly patients and also to compare the predictive accuracy of the Status Epilepticus Severity Score (STESS) and Epidemiology-based Mortality Score in Status Epilepticus — etiology, age, level of consciousness (EMSE-EAL) score for in-hospital mortality.
Methods: Eighty-five elderly patients (≥60 years of age) with a diagnosis of CSE were consecutively enrolled. The distinction between the score performances was determined by comparing the means area under the receiver operating characteristic curve (AUC).
Results: The mean age of respondents was 66.3 ± 7.4 years; the most common etiology of CSE was stroke (acute and remote symptomatic) in 48.2% of cases. In-hospital mortality was 16.5% in our series, and on multivariate analysis, variables significantly related with mortality were lack of response to first-line drugs (odds ratio (OR) = 43.05, 95% confidence interval (CI) = 4.7–386.8; p = .001) and higher EMSE-EAL score (OR = 0.08, 95% CI = 0.015–0.47; p = .005). On comparison, STESS with the cutoff value of ≥3 has AUC of 0.678 (95%CI = 0.54–0.81), whereas ESME-EAL with the cutoff value of ≥40 showed AUC of 0.901 (95% CI = 0.83–0.97).
Conclusions: Most frequent cause of CSE in elderly in our series was stroke and was also associated with high mortality. For the prediction of in-hospital mortality in elderly, EMSE-EAL-40 score is superior to STESS-3, which can be easily applied in resource-poor sectors with limited diagnostic facilities especially where continuous video-electroencephalogram (EEG) monitoring is unavailable.

1. Introduction

Status epilepticus (SE) is a neurological emergency and associated with significant morbidity and mortality. Acute seizures in the elderly present as SE in up to 30% of cases [1]. The most frequent etiology of SE in elderly consists of stroke, degenerative disease, infection, neoplasm, and trauma [2].

The age-specific incidence rate of SE has a bimodal distribution with peak incidence among infants and elderly. The average annual incidence rate of SE is about 15.5 per 100,000 patients between 60 and 69 years old, 21.5/100,000 in patients between 70 and 79 years old, and 24.9/100,000 in patients of 80 years and more [3–5]. Mortality steadily increases with advancing aging. Mortality for those over 60 years of age is 38%, approaching 50% in patients above 80 years of age [6,7].

Early understanding of the prognosis of SE episode is crucial in framing appropriate strategies for effective treatment. Thus, there is a need for the development of trustworthy tool for prognosis of SE among elderly for prompt therapeutic intervention.

The first score developed for the prediction of in-hospital mortality of convulsive status epilepticus (CSE) was the Status Epilepticus Severity Score (STESS) [8]. A subsequent scoring system published by Leitinger et al. was the Epidemiology-based Mortality Score in Status Epilepticus (EMSE) scoring system and was validated in a multicenter study, which included six variables for their prognostic value [9]. A version of EMSE including age, etiology, and level of consciousness (EMSE-EAL) was proposed by Pacha et al. [10].

In the last few decades, India, a rapidly developing nation, has experienced a dramatic demographic transition. According to Population Census 2011, there were nearly 104 million elderly persons (≥60 years of age) in India and is expected to increase to 173 million by 2026 [11,12]. Most of the elderly population (71%) resides in rural areas while 29% is in urban areas.

Uttar Pradesh, one of the biggest states is home for around 16.16% of Indian population, and the major proportion live in rural and remote places. There is lack of enough research evidence about clinical and

☆ Ethical approval: The study is in accordance with the ethical standards of the institution.We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Table 1
Univariate regression analysis of CSE outcome.

Demographic	Dead (%)14	Alive (%)71	Unadjusted OR (95% CI)	p value
Age	69.0 ± 9.6	65.8 ± 6.9	–	.24
Sex				
Male	10 (14.7)	58 (85.3)	0.56	.38
Female	04 (23.5)	13 (76.5)	1	
CSE type				
Generalized convulsive SE	4 (11.8)	30 (88.2)	0.54 (0.15–1.91)	.34
Focal onset evolving into bilateral convulsive SE	10 (19.6)	41 (80.4)	1	
History of epilepsy				
Yes	4 (10.3)	35 (89.7)	0.41 (0.11–1.43)	.155
No	10 (21.7)	36 (78.3)	1	
Duration of CSE in hours				
>12	6	12	3.68 (1.08–12.57)	**.03**
≤12	8	59	1	
Response to 1st line of treatment				
Nonresponder	7 (70.0)	3 (30.0)	22.6 (4.76–107.89)	<**.001**
Responder	7 (9.3)	68 (90.7)	1	
GCS				
≤8	11 (23.9)	35 (76.1)	3.77 (0.96–14.67)	**.045**
>8	3 (7.7)	36 (92.3)	1	
STESS				
>3	9 (22)	32(78.0)	2.19 (0.66–7.2))	.18
≤3	5 (11.4)	39 (88.6)	1	
EMSE				
>40	9 (40.9)	13 (59.1)	8.03 (2.30–27.9)	<**.001**
≤40	5 (7.9))	58 (92.1)	1	

Bold values indicates significance at p <.05.

epidemiological profile of SE in elderly patients. Hence, the present study was planned to study the clinical profile, etiologies, and outcome and also to compare the predictive accuracy of STESS and EMSE-EAL scores for in-hospital mortality in CSE in elderly.

2. Methods

A cross-sectional study was carried out by consecutively enrolling elderly patients (≥60 years of age) with the diagnosis of CSE admitted in the neurology department from December 2016 to February 2019. The study was subjected to review under the Institutional Ethical Review Board.

Convulsive status epilepticus was defined as continuous seizure activity lasting ≥30 min or recurrent seizure activity lasting ≥30 min without regaining of the preexisting level of consciousness [12]. Patients aged below 60 years, those with psychogenic CSE, hypoxia-related CSE, and nonconvulsive SE were excluded.

During the study period, a total of 315 patients were admitted with a diagnosis of CSE, of which 85 patients aged ≥60 years fulfilled the inclusion criteria and enrolled for the study.

Demographic data recorded included the following: age, gender, level of consciousness assessed by the Glasgow Coma Scale (GCS) at the time of admission, past history of epilepsy, duration and etiology of CSE, complications, and duration of hospital stay. The investigative data included laboratory tests (e.g., blood gas analysis, blood glucose, electrolyte levels, and tests of liver and renal function and Cerebrospinal Fluid (CSF) examination). Computer tomography (CT) and Magnetic resonance imaging (MRI) were done based on clinical indications and affordability. Electroencephalogram (EEG) recording was done within 12 h of cessation of CSE. Therapeutic drug monitoring and continuous video-EEG recording were not carried out.

Based on the semiologic description, all CSE events were classified according to the International League Against Epilepsy (ILAE) guidelines [13]. Based on history, laboratory testing, neuroimaging, and EEG, CSE etiologies were determined. Etiology of CSE was classified as established epilepsy, acute symptomatic, remote symptomatic, and cryptogenic (cause undetermined) [14].

First-line drugs used for the treatment were intravenous lorazepam and phenytoin as per the standard protocol; second-line drugs were valproate or levetiracetam. The patient received general anesthesia (coma induction) with either propofol or midazolam (3rd step) if CSE persisted. Appropriate management of the underlying medical/neurological condition was done. Based on clinical termination of the convulsion, the response to the treatment was delineated. Lack of response to the first-line of drugs was labeled for those whose seizures failed to respond to initial dosing of intravenous lorazepam and phenytoin.

The STESS has four parameters: level of consciousness, "worst" seizure type, age, and history of previous seizures. The score ranges from 0 to 6; a score of three points or more indicates the risk of mortality. Because of the unavailability of continuous video-EEG monitoring at our center, we used the modified version of EMSE including 3 variables, EMSE-EAL. For the prediction of in-hospital mortality, the optimal cutoff points was 3 for STESS and 40 for EMSE-EAL scores.

2.1. Outcome

The outcome was classified as in-hospital mortality or discharge from the hospital. In-hospital mortality was the primary outcome parameter of STESS and EMSE-EAL.

3. Statistical analysis

Statistical analyses were performed using IBM SPSS-23. Continuous data such as duration of epilepsy and stay in hospital was expressed in terms of mean, standard deviation, median, interquartile range (IQR), and percentage. The odds ratio (OR) was calculated using univariate logistic regression with a 95% confidence interval (CI), significant variables further considered for multiple logistic regression for estimation of adjusted odds ratio to determine significant prognostic factors among patients with CSE. Receivers operating characteristic (ROC) curves were generated for both the scales against the outcome to assess the cutoff values and respective sensitivity and specificity of scales as well as positive and negative predictive values. All tests were performed two-tailed. p-Values <.05 were estimated as significant.

4. Results

Among the 85 patients, 68 (80%) were male and the mean age was 66.3 ± 7.4 years (range: 60–90 years). Thirty-nine (45.9%) patients

Table 2
Etiology of CSE compared with outcomes.

Etiology	Total number of patients (%)	Alive (%)	Dead (%)
Established epilepsy			
Noncompliance	7(100)	6(85.7)	1(14.3)
Acute symptomatic			
CNS infections			
Neurocysticercosis	5(100)	5(100)	0(0)
Tuberculoma/TBM	1(100)	0	1(100)
Vascular			
Hemorrhage	9(100)	4(44.5)	5(55.5)
Infarct	8 (100)	5(62.5)	3(37.5)
Metabolic			
Hyponatremia	2(100)	2(100)	0(0)
Hypoglycemia	2(100)	2(100)	0(0)
Hyperglycemia	2(100)	2(100)	0(0)
Alcohol	2(100)	2(100)	0(0)
Remote symptomatic			
Posttraumatic	9(100)	8(88.9)	1(11.1)
Poststroke	24(100)	21(87.5)	3(12.5)
Small calcified lesion	2(100)	2(100)	0(0)
Cryptogenic	12(100)	12(100)	0(0)

Table 3
Predictors for mortality: multivariate analysis.

	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p value
Duration of CSE	3.68 (1.08–12.57)	0.529 (0.08–3.17)	.48
Lack of response to First Line drug	22.6 (4.76–107.89)	43.05 (4.7–386.8)	**.001**
GCS ≤ 8	3.77 (0.96–14.67)	4.29 (0.69–26.4)	.11
EMSE > **40**	8.03 (2.30–27.9)	0.08 (0.015–0.47)	**.005**

Bold values indicates significance at p <.05.

had preexisting epilepsy. Eight patients were aged over >80 years. The median duration of CSE was 5 h (IQR: 3–9; range: 1 to 31 h). There were no significant differences between the duration of hospital stay among those who survived (5.13 ± 2.7 days vs. 5.57 ± 2.31 days) than those who died. Univariate regression analysis of the CSE outcome is shown in Table 1.

Convulsive status epilepticus responded well with first-line drugs in seventy-five patients while ten patients required second-line and anesthetic drugs. The most common etiologies of CSE were stroke (acute and remote symptomatic) in 48.2% of patients followed by posttraumatic in 10.6% of patients. Noncompliance of Antiepileptic drugs (AEDs) was reported in 8.2% of patients. Neurocysticercosis accounted for 8.2% cases of the central nervous system (CNS) infections. Etiology of CSE is compared with outcomes in Table 2.

4.1. Mortality

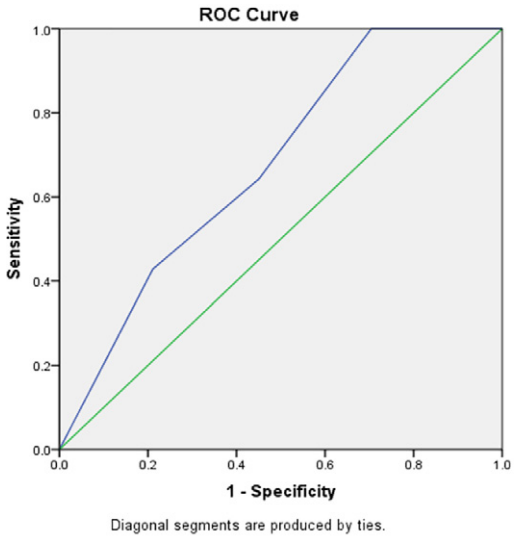
In-hospital mortality was 16.5% (n = 14) in our series; among them, acute stroke was the most common cause of mortality (n = 8) followed by poststroke (n = 3), posttraumatic (n = 1), noncompliance (n = 1), and CNS infection (n = 1) cases. Variables significantly associated with case fatality on univariate logistic regression analysis were as follows: duration of CSE, lack of response to first-line drugs, low GCS, and high EMSE score. On multivariate analysis, variables significantly related with mortality were lack of response to first-line drugs (OR = 43.05, 95% CI = 4.7–386.8; p = .001) and higher EMSE score (OR = 0.08, 95% CI = 0.015–0.47; p = .005) Table 3. There was no significant difference in mortality in reference to age, sex, or prior history of epilepsy.

The average STESS in survivors was 3.37 ± 1.12 in contrast to 4.07 ± 0.91 in dead. The sensitivity and specificity of STESS with the cutoff value of ≥3 were 62.2% and 54.9%, respectively with area under the receiver operating characteristic curve (AUC) of 0.678 (95% CI = 0.54–0.81). However, ESME-EAL with the cutoff value of ≥40 showed sensitivity and specificity of 64.2% and 81.6%, respectively, with the AUC of 0.901 (95% CI = 0.83–0.97). The ROC curves for the prediction of in-hospital mortality are depicted in Fig. 1.

5. Discussion

Among patients with SE, the elderly constitute the major and fastest-growing population. Despite of that, there is a dearth of literature on etiology and outcome of CSE in the elderly from Asia especially from the rural population of developing countries like India where healthcare facilities are already profoundly deficient.

Etiologies mainly establish the prognosis and mortality of SE and are age-dependent. In our series, the most frequent cause of CSE in elderly was stroke (acute and remote symptomatic) in 48.2% cases followed by posttraumatic in 10.6% cases. Rohracher A et al. also reported that vascular etiology was the most frequent cause of SE in elderly and



AUC - ROC = 0.678 ± 0.069 (p =0.037)

Sensitivity = 62.2%

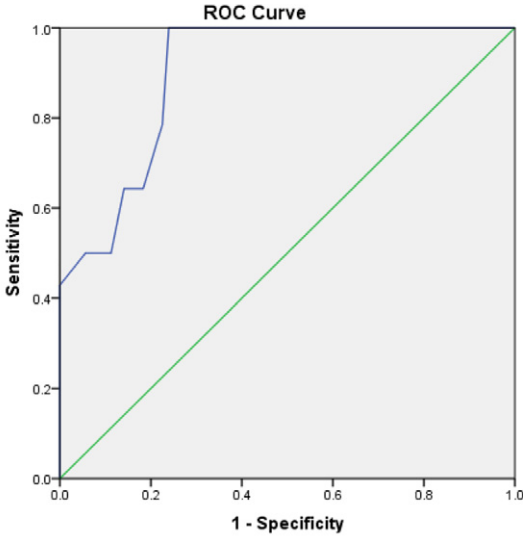
Specificity= 54.9%

PPV = 21.95%

NPV = 88.63%

Positive Likelihood ratio = 1.37

Negative Likelihood ratio =0.68



AUC -ROC = 0.901 ± 0.035 (p < 0.001)

Sensitivity = 64.2%

Specificity= 81.6%

PPV = 40.9%

NPV = 92.0%

Positive Likelihood ratio= 3.48

Negative Likelihood ratio = 0.43

Fig. 1. The ROC curves for the prediction of in-hospital mortality for STESS-3 and EMSE-40.

often in patients without preexisting epilepsy [15]. In a study from Richmond, Virginia, 35% of SE was caused by acute stroke and 26% by remote stroke; altogether, 61% of cases of SE were secondary to stroke in elderly population [16].

The in-hospital mortality in CSE among elderly was 16.5% (n = 14), and stroke was the leading cause of mortality in 78.5% (n = 11) of cases. After the acute stroke, SE had a noteworthy effect on both mortality and functional outcome [17]. Patients with SE of cerebrovascular origin had notably 2.12 times higher risk of long-term fatality, in comparison with patients with acute stroke without seizure [18]. In contrast, Jayalakshmi et al. reported vascular etiology as the most important cause of generalized CSE in elderly but was not related with the progression of CSE to refractory SE or with mortality [19].

Another predictor for mortality in our series was a lack of response to first-line treatment although not related to time of initiation of treatment. In about 30% of SE cases, refractory SE occurs and is associated with higher morbidity and mortality rates when compared with nonrefractory cases. Refractory CSE is associated with poor outcome in elderly patients [20] and may lead to death in 76% of cases [21].

In this communication, we compared STESS-3 and EMSE-EAL-40 scores for outcome prediction in CSE in elderly. The STESS is simple to apply and includes overall less clinical information. It is good at foretelling bad outcome but has a ceiling effect particularly in patients older than 65 years without a history of previous seizures [22]. The EMSE-EAL score can be calculated almost as simply as STESS. The possibility of ceiling effect was claimed to be lower for EMSE [23]. Etiology, which is not incorporated into STESS, is one of the variables in the modified version of EMSE-EAL. Pacha et al. [10] observed that the best combination of EMSE score variables was given excluding comorbidity as a variable. He also reported no statistical differences between the Charlson Comorbidity Index score in the survival group and nonsurvival group.

The STESS-3 showed a lower specificity than EMSE-EAL-40 score (54.9 vs. 81.6) in our series. In comparison with EMSE-EAL-40 with AUC of 0.901 (95% CI = 0.83–0.97), STESS-3 has AUC of 0.678 (95% CI = 0.54–0.81) and was associated with the lower rates of correct outcome prediction. Reindl et al. also reported that EMSE-EAL-40 showed significantly higher specificity (77.0 vs. 47.3%) in contrast to STESS-3 in a cohort of SE [24]. Our findings suggest that EMSE-EAL-40 tended to yield the superior rate of correctly classified episodes in elderly with CSE.

The limitation of the present study is the use of a modified version of EMSE, which has the lower positive predictive values than EMSE-EACE (etiology-age-comorbidity-EEG) [9]. Only motor CSE was included, and continuous video-EEG monitoring could not be done because of its nonaccessibility at our center.

Finally, the most frequent cause of CSE in elderly was stroke in our rural setup and was also related with high mortality; other predictor of mortality was lack of response to first-line treatment. For the prediction of in-hospital mortality in elderly, EMSE-EAL-40 score is superior to STESS-3, which can be easily applied in resource-poor sectors with limited diagnostic facilities especially in rural and remote setups where continuous video-EEG monitoring is unavailable.

Declaration of competing interest

None of the authors has any conflict of interest to disclose.

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