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Predicting Mortality in Status Epilepticus: Elixhauser Comorbidity Index and SOFA in ICU

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ABSTRACT

High mortality rates in status epilepticus (SE) within intensive care units (ICU) underscore the need for effective predictive scores to improve patient outcomes. While SE-specific scoring systems are commonly used, the role of comorbidity indices in mortality prediction is less explored.

This study assesses the prognostic efficacy of various scoring systems in predicting hospital mortality among critically ill SE patients in the ICU.

We conducted a retrospective analysis of 103 SE patients treated in the ICU at Harran University Medical Faculty Hospital from 2013 to 2023. Patients with myoclonic seizures due to cardiac arrest were excluded. The key scoring systems analyzed included the Elixhauser Comorbidity Index (ECI), Status Epilepticus Severity Score (STESS), END-IT (Encephalitis, Non-convulsive SE, Diazepam resistance, Image abnormalities, and Time to first treatment), Acute Physiology and Chronic Health Evaluation-II (APACHE II), and the Sequential Organ Failure Assessment (SOFA) scores. Univariate and multivariate logistic regression, along with ROC curve analysis, were used to identify mortality predictors.

Out of 103 patients, 54 met the study criteria, with 29 (54%) hospital deaths. Univariate analysis identified ECI, mRS, GCS, STESS, END-IT, APACHE II, and SOFA as significant mortality predictors. Multivariate analysis showed that ECI and SOFA were strong independent predictors. SOFA had an AUC of 0.848, close to ECI's 0.875 in predicting mortality. ECI and SOFA scores emerged as superior predictors of mortality in ICU patients with SE, suggesting that a broader approach considering systemic illness and comorbidities is crucial for prognosis, beyond SE-specific scoring systems.

Keywords: Status epilepticus; prognosis; comorbidity; intensive care units; critical illness

Introduction

Research on seizures in critically ill patients treated in intensive care units (ICU) indicates that anywhere from 1% to 40% of critically ill patients may experience seizures (1). Status epilepticus (SE) frequently emerged among half of all ICU patients presenting with seizures (2). Patients who develop SE while hospitalized in the ICU are more likely to have a more severe course of SE. The mortality rate among those patients ranges from 17 to 67% and they are more likely to experience refractory episodes (3-5). Therefore it is important to anticipate these patients with poor prognoses and act quickly in their treatment.

There are a lot of independent variables affecting SE outcome. The severity of SE, systemic illness, and comorbidities of patients are some of the variables. Researchers have been focused on finding the best scoring system to predict mortality in SE for quite some time. SE-specific scoring systems are the most commonly studied. In recent years, it has been suggested that systemic illness severity indexes can also be used to estimate mortality in SE patients in the ICU. In addition, comorbidity indexes also give information about patient's prognosis (6-9).

In the existing literature, no study has yet evaluated all 3 situations (the severity of SE, systemic illness, and comorbidity) together on mortality in patients with SE in the ICU. Therefore, our objective was to evaluate the prognostic accuracy of the severity of SE, systemic illness, and comorbidity scores and identify the most useful score for predicting hospital mortality in patients with SE in the ICU.

Materials and Methods

Study Design: A retrospective analysis of the data acquired from the patients with SE in the ICU clinic of Harran University Medical Faculty Hospital between 2013-2023 was performed. The study was approved by the local ethics committee of Harran University Medical Faculty with

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HRU/24.05.13 number and also complies with the Declaration of Helsinki.

Data Collection: Patients aged ≥ 18 years, who experienced SE while in the ICU were included in the study. Patients with myoclonic seizures due to cardiac arrest and nonconvulsive status epilepticus were excluded from the study. SE was defined as a seizure lasting longer than 5 minutes or recurrent seizures without regaining consciousness between episodes, consistent with the published guidelines (10).

Demographic variables, seizure etiology which was categorized as acute symptomatic, remote, progressive, and cryptogenic (10), calculated the Elixhauser Comorbidity Index (11), Status Epilepticus Severity Score (STESS) (8) and Encephalitis, Non-convulsive status epilepticus (NCSE), Diazepam resistance, Image abnormalities, and Time to first treatment (END-IT) (12), the Acute Physiology and Chronic Health Evaluation II score (APACHE Ⅱ) (13), and the Sequential Organ Failure Assessment (SOFA) score (14), the Modified Rankin scale (mRS) (15), Glasgow coma scale (GCS) (16) were recorded. The scores were calculated retrospectively. The EEG data obtained from recordings taken after the occurrence of status epilepticus have been documented.

Statistical Analysis: All statistical analyses were performed using SPSS statistical software, version 25 (IBM Inc., NC, USA). Categorical variables were presented as numbers and the frequency in percentages (%), while continuous variables were presented as median and interquartile range (IQR). Independent samples t-tests were conducted for normally distributed continuous variables, while the Mann-Whitney U test was used for non-normally distributed continuous variables. The Chi-square test was applied to categorical variables. Univariate and multivariate logistic regression analyses were performed to assess predictors of mortality. For the prediction of mortality in SE patients, all scores with p-values < 0.05 from the univariate analysis were included in the multivariate analysis using the stepwise (Wald) method. Odds ratios with 95% confidence intervals were calculated to assess the strength of association between independent variables and mortality. Receiver operating characteristics (ROC) curve analyses were performed to evaluate the predictive performance of scores for mortality. The optimal cut-off points were determined based on the maximum value of the Youden index (sensitivity + specificity - 1), maximizing both sensitivity and specificity. For each cut-off value, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Results were deemed statistically significant at a p-value < 0.05, with two-sided testing applied across all analyses.

A post-hoc power analysis was conducted using G*Power 3.1 to assess whether the sample size was sufficient for the logistic regression analysis. Based on a total sample size of 54 patients, a 50% mortality rate, an odds ratio of 1.253, and a significance level of 0.05, the power of the study was calculated to be 81.52%.

Results

From the initial cohort of 103 patients, 54 met the predefined inclusion criteria and were thus included in further analysis (Figure 1).

29(54%) patients died in the hospital. The demographic and clinical features of the survival and non-survival patients are demonstrated in Table 1. There were 12 patients with drug-resistant epilepsy among the epilepsy patients in this study. Of these, 5 were in the non-survival group, and 7 were in the survival group.

ECI, mRS, and GCS at admission, STESS, END-IT score, APACHE Ⅱ score, and SOFA score were statistically significant in univariate logistic regression for mortality as demonstrated in Table 2. Multivariate analysis showed that ECI and SOFA scores were predictors of mortality (p=0.004, p=0.006; respectively).

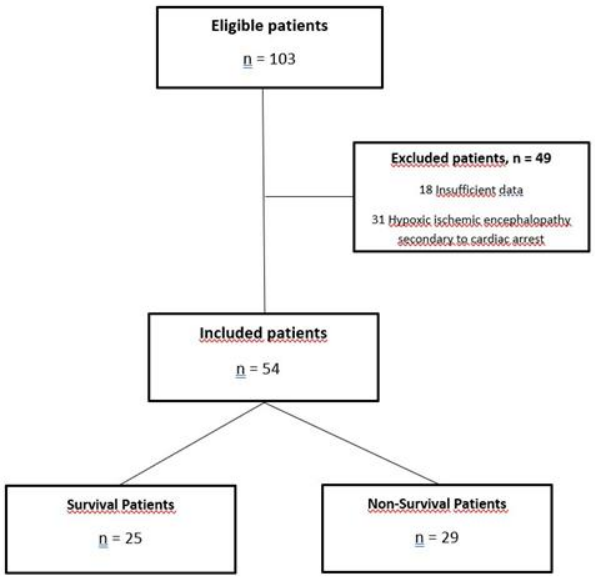

Fig. 1. Flowchart of the Patient Selection

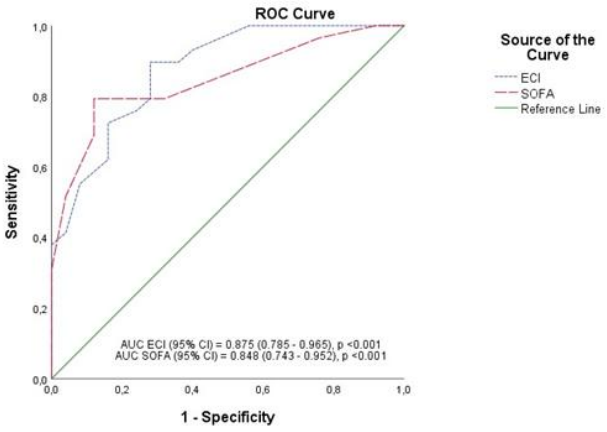

Fig. 2. Receiver operating characteristic (ROC) curves of the predictive model of ECI, and SOFA for mortality.
Abbreviations: AUC= Area under the curve, CI= Confidence Interval, ECI = Elixhauser Comorbidity Index; SOFA = Sequential Organ Failure Assessment

The area under the curves (AUCs) of the ROC curve for ECI and SOFA scores are illustrated in Figure 2. The ECI, with an AUC of 0.875, performs slightly better than the SOFA score, with an AUC of 0.848.

The optimal threshold, sensitivity, specificity, PPV, NPV, and accuracy of the predictive performance for mortality are revealed in Figure 3. In this analysis, the ECI demonstrates lower sensitivity (72%) compared to SOFA (88%)

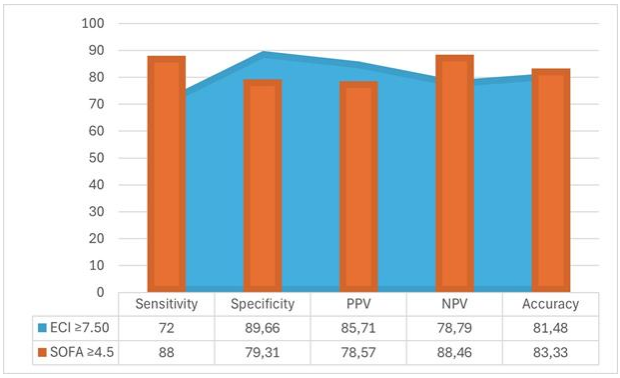

Fig. 3. Predictive performance for mortality of ECI and SOFA at their respective best cut-off values.
Abbreviations: ECI = Elixhauser Comorbidity Index; SOFA = Sequential Organ Failure Assessment; PPV = Positive Predictive Value; NPV = Negative Predictive Value

but higher specificity (89.66%) than SOFA (79.31%).

Discussion

Within critically ill patient populations diagnosed with SE, this study investigated the predictive capabilities of seizure severity, illness severity, and comorbidity scores for hospital mortality specifying that ECI and SOFA are the strongest scores predicting mortality. In previous research, scales measuring the severity of SE, such as STESS and EMSE, have proven insufficient to predict mortality. Therefore, more robust models designed to predict outcomes have included disease severity scores such as SOFA, APACHE Ⅱ, Inflammation, Nutrition, Consciousness, Neurological function and Systemic condition (INCNS), and Simplified Acute Physiology Score II (SAPS II). Yet, none of the assessed scoring systems reached the accuracy required to guide individual clinical decisions independently (6,17-19). In these studies, comorbidity indexes were not incorporated into the models. Although the Charlson Comorbidity Index (CCI) and ECI are widely recognized risk adjustment tools, the most effective comorbidity score for SE patients has not yet been determined. ECI had a better discriminative performance compared to the CCI for predicting mortality in patients with some diseases such as stroke, COVID-19, and schizophrenic disorders (20-22). Also, the ECI outperformed the CCI by 60% in mortality prediction in patients after orthopedic surgery (23). Hence we determined to study ECI and established that it serves as a predictor of mortality with SE patients in the ICU.

Table 1: Demographic and Clinical Features of the Survival and Non-Survival Patients with SE in ICU

	Survival	Non-Survival	p
	n = 25	n=29	
Age, m (IQR)*	33 (36)	45 (42,5)	0.142
Gender, n, (%) ¥			
Female	10 (40)	12 (41)	1
Male	15 (60)	17 (59)	
Epilepsia History, n ¥	15	6	**0.007**
Age at epilepsy onset, m (IQR)*	13 (34)	10 (15)	0.507
Number of antiepileptic drugs, m (IQR)*	1 (2)	0 (0)	**0.020**
ECI, m (IQR)*	5 (10,5)	17 (11,5)	**0.001**
mRS at admission, m (IQR)*	4 (0,5)	4 (1)	**0.004**
GCS at admission, m (IQR)#	12 (3,5)	7 (5,5)	**0.001**
APACHE Ⅱ score, m (IQR)*	3 (4,5)	8 (4,5)	**0.001**
SOFA score, m (IQR)*	3 (1,5)	7 (4)	**0.001**
Duration of stay in ICU, m (IQR)*	5 (5)	14 (25)	**0.009**
Etiology, n ¥			
Remote	6	1	
Acute Symptomatic	14	27	**0.006**
Cryptogenic	5	1	
Seizure Type, n ¥			
Focal	5	9	0.546
Generalized	19	19	
Refractory SE, n ¥	2	16	**0.001**
STESS, m (IQR)*	0 (2)	2 (2)	**0.004**
END-IT score, m (IQR)*	0 (1)	2 (2)	**0.001**
Abnormal NE, n ¥	2	26	**0.001**
Altered level of consciousness, n ¥	13	16	1
Todd Paresis, n ¥	7	10	0.828
Abnormal EEG, n ¥	13	8	0.120
Intubation, n ¥	5	29	**0.001**
Anesthetic medication, n ¥	2	16	**0.001**
Inotropic Agents, n ¥	1	28	**0.001**

Independent Samples T Test
*Mann Whitney-U Test
¥ Chi-Square Test
Abbreviations: SE = Status Epilepticus; ICU = Intensive Care Unit; n = number of patients; m = median; IQR = Interquartile Range; ECI = Elixhauser Comorbidity Index; mRS = Modified Rankin Score; GCS = Glasgow Coma Scale; APACHE-Ⅳ = Acute Physiology and Chronic Health Evaluation-Ⅳ; SOFA = Sequential Organ Failure Assessment; ICU = Intensive Care Unit; STESS = Status Epilepticus Severity Score; END-IT = Encephalitis, Non-convulsive status epilepticus, Diazepam resistance, Image abnormalities, and Tracheal intubation; NE = Neurological Examination; EEG = Electroencephalography.

STESS, the initial and most frequently utilized severity score for SE, demonstrates limited predictive accuracy (8,17,24). The STESS effectively predicts survival in SE patients instead of mortality (8,25). The END-IT score originated from a study involving a young cohort of Asian patients with convulsive status epilepticus, where encephalitis was the cause in over a third of cases, and many required mechanical ventilation (12). While the END-IT score was primarily developed to predict functional outcomes rather than mortality, it has been suggested that it indirectly gauges mortality risk by considering factors linked to poor outcomes such as diazepam resistance and

Table 2: Binary Logistic Regression for Mortality

	Univariate		Multivariate (Stepwise)	
	OR (%95 CI)	p	OR (%95 CI)	p
Elixhauser Comorbidity Index	1.253 (1.117 - 1.405)	**0.001**	1.203 (1.061 – 1.364)	**0.004**
mRS at admission	3.576 (1.375 - 9.302)	**0.009**		
GCS at admission	0.661 (0.516 - 0.847)	**0.001**		
STESS	1.649 (1.07 - 2.541)	**0.023**		
END-IT Score	4.389 (2.046 - 9.415)	**0.001**		
APACHE Ⅱ Score	1.451 (1.174 - 1.793)	**0.001**		
SOFA Score	2.134 (1.431 - 3.181)	**0.001**	1.865 (1.196 – 2.906)	**0.006**
Constant			0,009	**0.001**

Accuracy = %87; Cox&Snell R^2=0.500; Nagelkerke R^2=0.668

Abbreviations: OR = Odds Ratio; CI = Confidence Interval; mRS = Modified Rankin Score; GCS = Glasgow Coma Scale; STESS = Status Epilepticus Severity Score; END-IT = Encephalitis, Non-convulsive status epilepticus, Diazepam resistance, Image abnormalities, and Tracheal intubation; APACHE-Ⅳ = Acute Physiology and Chronic Health Evaluation-Ⅳ; SOFA = Sequential Organ Failure Assessment.

tracheal intubation (26). Given the differences in parameters between the STESS and END-IT, Yuan et al. suggested that future research should explore whether combining these scores enhances their predictive accuracy (27). In our study, although both STESS and END-IT showed statistical significance in univariate analysis, multivariate analysis showed that combining these scores did not predict mortality.

While SE is considered a neurological emergency, there is increasing evidence to suggest that it is also a multisystemic illness, affecting several systemic organs simultaneously (28). Numerous studies indicate a significant correlation between the APACHE Ⅱ score and mortality in patients with SE (8,19); however, discrepancies in its predictive accuracy also exist (29-31). For patients with post-cardiac arrest syndrome, the SOFA score accurately predicts mortality at 28 days (32). In patients receiving ICU treatment for refractory status epilepticus (RSE), the SOFA score served as an independent predictor of hospital mortality (33). In the present study, multivariate regression analysis revealed that SOFA and ECI scores were independent predictors of hospital mortality. This implies that the presence of systemic diseases and comorbidities is more critical than the severity of SE in assessing the prognosis of SE.

The ECI is more effective in ruling out disease due to its higher specificity, making it particularly useful in identifying healthy individuals. Conversely, the SOFA score, with its higher sensitivity, is better suited for ruling in disease, as it is more capable of detecting patients who actually have the condition. This distinction in their diagnostic strengths highlights the different clinical applications where each index may be most appropriately utilized.

Limitations: Despite novel insights into the predictive accuracy of scoring systems for SE in ICUs, this study carries limitations typical of its retrospective design. Moreover, the sample might have been insufficient to achieve enough statistical power to adequately cover the spectrum of SE manifestations and states across different ICUs. Despite these limitations, our study holds significance as it represents the first investigation wherein comorbidities were assessed using the ECI and corresponding cut-off values were established.

This study represents a comprehensive evaluation of the prognostic utility of various scoring systems, encompassing the severity of SE, systemic illness, and comorbidities in predicting hospital mortality among critically ill patients with SE in an ICU setting. Our findings underscore the significant role of systemic disease and comorbidities, as reflected by the ECI and the SOFA score, in determining outcomes for these patients. These indices outperformed traditional SE-specific scores such as the STESS and the END-IT score, highlighting the necessity for a more holistic approach in the assessment and management of SE.

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Statements and Declarations

Conflict of Interest: The authors declare that they have no conflict of interest.

Status of Ethical Clearance: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the local ethics committee of Harran University Medical Faculty in 2024 (protocol number: HRU/24.05.13).

Availability of Data and Material: Patients' data is only available from the corresponding author on a reasonable request.

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