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Prognostic Value of the Status Epilepticus Severity Score in Clinical Outcomes

Status Epileptikus Şiddet Skorunun Klinik Sonuçlardaki Prognostik Değeri

Tulin Gesoglu Demir*[1], Firat Celik[1], Murat Cekic[1], Ozlem Ethemoglu[1], Adalet Gocmen[2]

[1]Department of Neurology, Harran University Faculty of Medicine, Şanlıurfa /Türkiye,
[2] Department of Neurology, Şanlıurfa Education and Research Hospital, Şanlıurfa /Türkiye,

Abstract

Background: Status epilepticus (SE) is a neurological emergency associated with high morbidity and mortality. The Status Epilepticus Severity Score (STESS) has been proposed as a prognostic tool to predict outcomes in SE patients. This study aims to evaluate the effectiveness of STESS in predicting clinical outcomes and in-hospital mortality rates among SE patients.

Materials and Methods: We conducted a retrospective analysis of patient data collected between January 2020 and February 2024 at Harran University Faculty of Medicine Hospital. The study included 29 patients diagnosed with SE, who were categorized based on etiological factors and treatment modalities. STESS was calculated for each patient, and its correlation with clinical outcomes and mortality rates was analyzed using statistical methods.

Results: The mean age of the study group was 37.55±18.81 years, and the mortality rate was 13.8% (n=4). Acute symptomatic etiology played a 31% role in the overall etiology. The most common etiology was central nervous system (CNS) infections (17.2%) and the most common comorbidity was DM (17.2%). 13.8% of the patients died during follow-up. There was no significant difference between the survivors and the deceased patients in terms of mean age, duration of hospitalization and duration of status (p>0.005). The mean STESS score of the patients was 1.48±1.05. Age was significantly higher in patients with STESS scores 3-6 (p=0.004). Mortality was significantly higher in patients with higher STESS scores (p=0.005). The sensitivity of STESS in predicting mortality was 95.7%, specificity was 50% and PPV 75%, NPV 12%.

Conclusion: The study demonstrates the prognostic value of STESS in predicting clinical outcomes in SE patients. Utilizing STESS in clinical practice can help identify high-risk patients and guide therapeutic strategies to improve patient outcomes. Further research is warranted to validate these findings in larger, multi-center studies.

Keywords: Status Epilepticus, STESS, Prognosis, Mortality, Clinical Outcomes

ÖZ

Amaç: Status epileptikus (SE), yüksek morbidite ve mortalite ile ilişkili bir nörolojik acil durumdur. Status Epileptikus Şiddet Skoru (STESS), SE hastalarında sonuçları öngörmek için önerilen bir prognostik araçtır. Bu çalışmanın amacı, STESS'in SE hastalarında klinik sonuçları ve hastane içi mortalite oranlarını öngörmedeki etkinliğini değerlendirmektir.

Gereç ve Yöntem: Ocak 2020 ile Şubat 2024 tarihleri arasında Harran Üniversitesi Tıp Fakültesi Hastanesi'nde toplanan hasta verilerinin retrospektif bir analizini yaptık. Çalışmaya, etiyolojik faktörlere ve tedavi yöntemlerine göre kategorize edilen SE tanısı konmuş 29 hasta dahil edilmiştir. Her hasta için STESS hesaplandı ve klinik sonuçlar ve mortalite oranları ile korelasyonu istatistiksel yöntemler kullanılarak analiz edildi..

Bulgular: Çalışma grubunun yaş ortalaması 37,55 ± 18,81olup mortalitenin %13,8 (n=4) olduğu, etiyolojide akut semptomatik etiyolojinin %31 rol oynadığı belirlendi. Saptanabilen etyolojide en sık merkezi sinir sistemi (MSS) infeksiyonlarına rastlandı (% 17.2). En sık komorbidite olarak ise DM'e rastalandı (% 17.2). Hastaların %13,8'i takipte öldü. Hayatta kalanlarla ölenler arasında ortalama yaş, hastanede yatış süresi ve status süreleri açısından anlamlı farklılık yoktu (p>0,005) Hastaların STESS skoru ortalamaları 1,48 ± 1,05 idi. STESS 3-6 puan alanlarda yaş anlamlı olarak daha yüksekti (p=0,004). STESS skoru yüksek olan hastalarda mortalite anlamlı olarak daha yüksek olduğu gözlendi (p=0.005). STESS'nun mortaliteyi ön görmedeki duyarlılığı %95,7, özgüllüğü %50 ve PPV %75 NPV %12 olduğu bulundu.

Sonuç: Çalışma, STESS'in SE hastalarında klinik sonuçları öngörmedeki prognostik değerini göstermektedir. Klinik uygulamada STESS'in kullanılması, yüksek riskli hastaların belirlenmesine ve tedavi stratejilerinin yönlendirilmesine yardımcı olabilir. Bu bulguları daha geniş, çok merkezli çalışmalarda doğrulamak için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: Status Epileptikus, STESS, Prognosis, Mortalite, Klinik Sonuçlar

Highlights

- Higher Status Epilepticus Severity Score (STESS) is associated with increased mortality, indicating its prognostic value in clinical outcomes.
- Acute symptomatic etiology was found to be the most common cause of SE, with central nervous system infections.
- STESS showed a high sensitivity in predicting mortality, making it a valuable tool for identifying high-risk SE patients and guiding treatment strategies.

***Corresponding author:** Tulin GESOGLU DEMIR, Address: Harran University Faculty of Medicine, Osmanbey, Sanliurfa/Turkiye **E-mail:** drtulindemir@gmail.com

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Introduction

Status epilepticus (SE) is a neurological emergency. SE's mortality rate ranges between 8.6% to 46.5% (1-4). It is difficult to treat as it is necessary to stabilize effectiveness and quickly stop seizures and toxicity to reduce complications. This difficulty is further increased by the heterogeneity of SE etiology, semiology and severity, and usually requires individualized treatment (5). In this context, evaluating the individual patient's prognosis as early as possible in the management of SE is very important to avoid overtreatment and its potentially harmful consequences or inadequate treatment (6). Prognostic scores furnish clinicians and families with predictive information regarding clinical outcomes. They provide a practical way to classify the severity of SE and guide individualized treatment (3). The Status Epilepticus Severity Score (STESS) has been proposed as a valuable and quick-to-use clinical prognostic scale that supports neurologic assessment for outcome prediction and developed by Rossetti et al.(7). The STESS is the first score used for SE prognosis classification based on four outcomes: level of consciousness, seizure type, age and seizure history. Rossetti et al. found an optimal cut-off value at ≥3 with a sensitivity of 0.94 and specificity of 0.60 in STESS with a maximum score of 6. The negative predictive value (NPV) was 0.97 and the positive predictive value (PPV) was 0.39 (7). The prognostic performance of STESS has been investigated in various studies and recently outlined in a meta-analysis, showing that it has a high NPV for short-term mortality but a very low PPV (5). In other terms, it is more influential in accurately forecasting patients who will survive but not as effective in forecasting death (8). A retrospective study by Ciurans et al. found that STESS was associated with inpatient mortality in 49 patients with refractory status epilepticus (RSE) in the intensive care unit (9). A report studying prognostic scores among 55 SE patients admitted to the neurology intensive care unit reported the STESS was sensitive but did not assess its prognostic value in terms of mortality (10).

The objective of this study was to assess the clinical findings, etiology and prognosis in SE and to determine the role of STESS in predicting prognosis and mortality.

Materials and Methods

During the period from January 2020 to February 2024, a total of 29 adult patients diagnosed with SE as a result of changes in mental status or seizures by a neurologist while hospitalized at Harran University Faculty of Medicine Hospital's neurology department or other clinics were part of the research study. Patients with anoxic-ischemic SE were excluded. The demographic and clinical features of the patients, as well as their prognosis and prognosis predictors, were recorded. SE is defined as a patient's neurologic status lasting longer than five minutes or having two or more sequential seizures without returning to baseline between seizures. RSE was described as SE that continued even after benzodiazepine and a minimum of two doses of parenteral antiepileptic therapy at proper doses. Super-refractory status epilepticus (SRSE) was described as SE lasting over 24 h despite treatment with antiepileptic drugs and anesthetics. Mortality was defined as in-hospital mortality, recorded from the time of admission to the hospital until death within the hospital. The diagnosis of non-convulsive status epilepticus (NCSE) was made in accordance with the Salzburg Consensus Criteria (11). Patients were also etiologically classified according to the International League Against Epilepsy (ILAE) SE classifications (12). To facilitate statistical analysis, factors likely to be associated with mortality were categorized and STESS was then calculated (7). A STESS score of 0 - 2 was considered indicative of a good prognosis, while a STESS score of 3 - 6 was associated with an poor prognosis. Two groups of outcomes were defined as 'return to baseline' and 'death'. The study was granted permission from the Ethics Committee of Harran University Faculty of Medicine (HRU/24.05.36), Date: 29.04.2024.

Statistical Analysis

Statistical analysis was performed using IBM SPSS for Windows version 20.0 package program. While evaluating the study data, frequencies (number, percentage) were given for categorical variables and descriptive statistics (mean, standard deviation) were given for numerical variables. The normality assumptions of the numerical variables were examined by Shapiro Wilk normality test. Mann Whitney U and Chi-square tests were used to compare categorical variables. In the comparison of numerical changes between independent groups, the Independent sample T Test was used for normally distributed variables. Statistical significance was interpreted at the ≤0.05 level. Sensitivity, specificity, PPV, NPV of STESS in predicting mortality were given.

Results

Our study included 29 SE patients, 12 (41.1%) females and 17 (58.6%) males. The mean age was 37.55±18.81 years (19-87). NCSE was diagnosed in 1 (3.4%), RSE in 25 (86.2%) and SRSE in 3 (10.3%) patients. 24 patients (82.7%) had a known history of epilepsy. While no etiology was identified in 44% (n=11) of the patients, acute symptomatic etiology was observed in 31% (n=9), progressive symptomatic etiology in 6.8% (n=2) and distant

symptomatic etiology in 24.1% (n=7). The most common etiologic cause was CNS infections (n=5, 17.2%) and the most common comorbid disease was DM (n=5, 17.2%). Mortality was 13.8% (n=4), and there was no additional mortality during follow-up. Of these patients, 2 (50%) were known to have had epilepsy previously. There was no significant difference between the survivors and the deceased patients in terms of mean age, duration of hospitalization and duration of status (p>0.005) **(Table 1).**

Table 1. Clinical characteristics of the survivors and non-survivors

Variables	Survivors	Non-survivors	*p*
Patients, n (%)	25 (86.2)	4 (13.8)	
Gender, n (%)			0.659
Male	15 (88.2)	2 (11.8)	
Female	10 (83.3)	2 (16.7)	
Age, year, mean ± SD	36.12 ± 18.92	46.50 ± 17.71	0.339
<65 years, n (%)	23 (92)	4 (100)	
>65 years, n (%)	2 (8)	0(0)	
Length of hospital stay (day)	6.68 ± 3.94	5.75 ± 2.50	0.553
Status duration (min)	109.40 ± 84.96	97.50 ± 66.52	0.764
History of epilepsy, n (%)			0.066
History of epilepsy (+)	22 (88)	2 (50)	
History of epilepsy (-)	3 (12)	2 (50)	
Comorbidities, n (%)			0.075
Comorbidity (+)	13 (52)	4 (100)	
Comorbidity (-)	12 (48)	0(0)	
Etiology, n (%)			0.075
Etiology determined	13 (52)	4 (100)	
Etiology not determined	12 (48)	0(0)	
Type of etiology, n (%)			
Cryptogenic	11 (44)	0 (0)	
Acute Symptomatic	6 (24)	3 (75)	
Progressive Symptomatic	2 (8)	0 (0)	
Distant Symptomatic	6 (24)	1 (25)	

The mean STESS score of the patients was 1.48±1.05. The mean age of patients with STESS scores 0-2 was significantly lower than the group with STESS scores 3-6 (p = 0.004). No significant difference was found in these groups in terms of length of hospitalization, duration of SE and comorbid diseases. Fifty percent (n=3) of patients with a STESS score of 3-6 and only 4.3% (n=1) of patients with a STESS score of 0-2 died. Mortality was significantly higher in patients with higher STESS scores (p = 0.005) **(Table 2).** The sensitivity of STESS in the context of mortality prediction was 95.7%, specificity was 50% and PPV 75%, NPV 12%. In the treatment of SE, 72.4% (n=21) of the patients received diazepam and 17.2% (n=5) received midazolam. The most commonly used second-line antiepileptic drug was IV levetiracetam (69%, n=20), the second most common drug was IV phenytoin (37.8% n=11), and the third most common drug was IV valproic acid (34.5% n=10). Of the 3 patients

evaluated as SRSE, 2 (6.9%) received thiopental and one received ketamine.

Table 2. Clinical characteristics according to STESS

Variables	Group 1 (STESS=0-2)	Group 2 (STESS=3-6)	*p*
Patients, n (%)	23 (79.3)	6 (20.7)	
Gender, n (%)			0.711
Male	10 (43.5)	2 (33.3)	
Female	13 (56.5)	4 (66.7)	
Age, year, mean (SD)	30.48±11.20	64.67±17.78	**0.004**
<65 years, n (%)	23 (100)	4 (66.7)	
>65 years, n (%)	0	2 (33.3)	
Length of hospital stay (day)	6.26±2.84	7.67±6.43	0.622
Status duration (min)	107.61±88.45	108.33±54.55	0.980
History of epilepsy, n (%)			0.827
History of epilepsy (+)	22 (95.7)	2 (33.3)	
History of epilepsy (-)	1 (4.3)	4 (66.7)	
Comorbidities, n (%)			**0.032**
Comorbidity (+)	12 (52.2)	5 (83.3)	
Comorbidity (-)	11 (47.8)	1 (16.7)	
Death, n (%)			**0.005**
Survivors	22 (95.7)	3 (50)	
Non-survivors	1 (4.3)	3 (50)	
Etiology, n (%)			**0.000**
Etiology determined	14 (60.9)	3 (50)	
Etiology not determined	9 (39.1)	3 (50)	
Type of etiology			
Cryptogenic	9 (39.1)	2 (33.3)	
Acute Symptomatic	5 (21.7)	4 (66.7)	
Progressive Symptomatic	2 (8.7)	0	
Distant Symptomatic	7 (30.4)	0	

Discussion

In this study, the significance of the STESS in prognostic assessment of SE patients was demonstrated. Our findings indicate that patients with higher STESS scores have significantly increased mortality. This study aligns with previous research showing variable SE outcomes and highlights the importance of using prognostic scores in guiding treatment strategies.

Several factors associated with poor outcome of SE include age ≥60 years (13), longer duration of SE (14), no past history of seizures (15), low Glasgow coma scale score at presentation (13, 15), type of SE (7), acute symptomatic etiology (16), and the presence of periodic lateralized epileptiform discharges on EEG (13). Prognostic scores are

valuable instruments for guiding the medical strategy and management of patients with SE (3). This study was conducted in a tertiary care hospital and it was observed that SE was more common in men and under 65 years of age, and CNS infection was the most common etiology in cases. The mortality rate was found to be high in cases with high STESS score.

Age is a predictor of mortality in SE patients (17). Although it is an unchangeable prognostic factor, age, which is a variable also included in STESS, should be taken into account in the overall evaluation. In our study, the mean age was lower compared to similar literature data and higher compared to male prevalence (18). In the present study, age was significantly higher in the group with STESS 3-6 ($p=0.004$). Advanced age (>65 years) has been shown as a poor prognostic factor in similar studies (19). In a study using STESS to predict clinical outcomes of SE, age and gender did not differ significantly between survivors and non-survivors (20). Reports on the sex of patients with SE are conflicting; some studies have shown a higher prevalence in males, whereas others have indicated a higher prevalence in females (21-23). In the current research, there was a higher prevalence of males.

The role of the underlying etiology is crucial in influencing short-term mortality, especially if it is acute and fatal (24). Like in previous studies, the current research also identified acute symptomatic etiology as the most common cause of SE. While CNS infection was the top reason for SE in Western China, strokes were more prevalent in the United States and certain developed European nations based on Zhou et al.'s study (25-27). This is linked to the elevated occurrence of CNS infections, particularly encephalitis and tuberculous meningitis in developing countries (25). Similarly, the presence (type and number) of comorbidities may influence short-term mortality and may indicate higher baseline frailty in patients who are less likely to survive. Identification and, if possible, treatment of comorbidities may improve prognosis and reduce mortality (28). In a case report, muscle damage in a patient with SE was noted and patients at risk of acute kidney injury were recommended to be closely monitored for creatinine kinase and urine output (29). A retrospective observational study in patients with RSE examined the impact of comorbidities on functional outcome and mortality and showed that STESS and chronic kidney disease were associated with mortality (9).

A retrospective study of prognostic assessment in SE patients in the ICU found that diabetes was strongly associated with mortality (30). A study on 173 patients with SE discovered that having diabetes increased the likelihood of in-hospital mortality (31). In a separate SE study (32), hyperglycemia was reported to be a predictor of poor outcome and has been suggested in connection with exacerbation of seizures and SE-induced hippocampal damage (33). In the present study, DM was the most common comorbid disease. The STESS score of those with comorbid diseases was significantly lower and all of those who died had at least one comorbid disease. While causality is uncertain, patients in the ICU with SE and diabetes may face complications such as extended intubation and sepsis as a result of high blood sugar levels. Managing high blood sugar levels in these patients continues to be crucial due to its adverse effects on critically ill patients (34).

Reliable prognostic indicators are needed to support the clinical approach and prevent both under- and over-treatment (35). With its convenience and ease of use, STESS has been commanly used to estimate SE outcomes and stratify patients (36). Former reports have shown that STESS is an important prognostic predictor (7). Different mortality rates have been reported in studies conducted with epilepsy patients (37, 38). In the current study, the acute symptomatic group had the highest mortality rate. Mortality rate was similarly in both sexes in the group with and without a history of epilepsy. In Göl et al.'s research, 48.5% of individuals with a STESS score of 3-6 died, compared to zero deaths in the group with a STESS score of 0-2 (39). Goyal et al. found a strong correlation between elevated STSS scores and negative neurological outcomes upon discharge, the requirement for inducing coma, and a lack of response to treatment within one hour. A STESS score of less than 3 had a high negative predictive value of 96.9% for mortality, 96.7% for poor neurological outcome at discharge, and 96.7% for requiring coma induction. On the other hand, a STESS score of less than 2 had a perfect negative predictive value of 100% for mortality, coma induction, and poor neurological outcome at discharge. (40). In the present study, 50% of patients with STESS scores of 4-6 and only 4.3% of patients with STESS scores of 0-3 died. Mortality was significantly higher in patients with higher STESS scores. The sensitivity of STESS in predicting mortality was 95.7%, specificity was 50% and PPV 75%, NPV 12%.

Study Limitations

As a limitation, in addition to its retrospective nature and limited number of patients, this study only assessed in-hospital mortality, did not include variables related to physical disability or long-term mortality and life quality after discharge. Furthermore, STESS scoring is based on physicians' judgment and may therefore introduce bias. There is a need for improved scales or indicators for the determination of the whole prognosis of patients with SE. Given the low primary outcome rates, the power analysis of the study is limited. Increasing the sample size in

future studies would enhance the generalizability of the findings and provide more robust conclusions.

Conclusion

Finally, in our research, it was noted that SE was more common in males and under 65 years of age, and CNS infection was the most frequent etiology in cases. The mortality rate was found to be high in cases with high STESS score. Underlying etiology, age and comorbidities are important determinants of prognosis. In the light of our data and the literature, low (<3) STESS has a good NPV for unfavorable results. In SE with low STESS, intensive treatment protocols can be avoided at least in the initial phase and treatment-related complications can be prevented. The STESS score is an easily applicable scoring tool that helps predict mortality.

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