Seizure 56 (2018) 92–97

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Comparison of scoring tools for the prediction of in-hospital mortality in status epilepticus

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ARTICLE INFO

Article history:
Received 10 December 2017
Received in revised form 29 January 2018
Accepted 30 January 2018
Available online xxx

Keywords:
Status epilepticus
Mortality
Outcome
STESS
EMSE
END-IT
mSTESS

ABSTRACT

Purpose: Several scoring tools have been developed for the prognostication of outcome after status epilepticus (SE). In this study, we compared the performances of STESS (Status Epilepticus Severity Score), mSTESS (modified STESS), EMSE-EAL (Epidemiology-based Mortality Score in Status Epilepticus-Etiology, Age, Level of Consciousness) and END-IT (Encephalitis-NCSE-Diazepam resistance-Image abnormalities-Tracheal intubation) in predicting in-hospital mortality after SE.

Method: Data collected retrospectively from a cohort of 287 patients with SE were used to calculate STESS, mSTESS, EMSE-EAL, and END-IT scores. The differences between the scores' performances were determined by means of area under the ROC curve (AUC) comparisons and McNemar testing.

Results: The in-hospital mortality rate was 11.8%. The AUC of STESS (0.628; 95% confidence interval (CI), 0.529–0.727) was similar to that of mSTESS (0.620; 95% CI, 0.510–0.731), EMSE-EAL (0.556; 95% CI, 0.446–0.665), and END-IT (0.659; 95% CI, 0.550–0.768; $p > .05$ for each comparison) in predicting in-hospital mortality. STESS with a cutoff of 3 was found to have lowest specificity and number of correctly classified episodes. EMSE-EAL with a cutoff at 40 had highest specificity and showed a trend towards more correctly classified episodes while sensitivity tended to be low. END-IT with a cutoff of 3 had the most balanced sensitivity-specificity ratio.

Conclusions: EMSE-EAL is as easy to calculate as STESS and tended towards higher diagnostic accuracy. Adding information on premorbid functional status to STESS did not enhance outcome prediction. END-IT was not superior to other scores in prediction of in-hospital mortality despite including information of diagnostic work-up and response to initial treatment.

1. Introduction

Status epilepticus represents a challenging condition in which therapy needs to be balanced between both the risks of over- and undertreatment. While the first may lead to iatrogenic harm [1–3], the latter carries the risk of prolonged seizure activity and thus neuronal damage [4]. Early knowledge on the prognosis of an SE episode might help differentiate patients in need of aggressive therapy from those in whom a conservative approach is justifiable [5]. To date, four prediction tools have been created aiming to allow for prognosis after SE based on different sets of prognosticators: 1) Status Epilepticus Severity Score (STESS) [6], 2) the modified STESS (mSTESS) [7], 3) Epidemiology-Based Mortality Score in Status Epilepticus (EMSE) [8], and 4) Encephalitis-NCSE-Diazepam resistance-Image abnormalities-Tracheal intubation (END-IT) [9]. In this study, these four scores were compared in an attempt to

Abbreviations: CI, confidence interval; mRS, modified Rankin Scale; SE, status epilepticus; STESS, Status Epilepticus Severity Score; mSTESS, modified STESS; EMSE-EAL, Epidemiology-based Mortality Score in Status Epilepticus – Etiology, Age, Level of Consciousness END-ITEncephalitis-NCSE-Diazepam resistance-Image abnormalities-Tracheal intubation.

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https://doi.org/10.1016/j.seizure.2018.01.024
1059-1311/

evaluate their predictive accuracy for in-hospital mortality in a cohort of SE patients.

2. Methods

2.1. Definitions

Following its operational definition [10,11] and in line with previous studies, SE was defined as clinical and/or electroencephalographic evidence of seizure activity for ≥5 min or as series of seizures with incomplete interictal clinical recovery [8,12]. An SE episode was defined as refractory when seizures persisted after application of two lines of therapy [13]. SE secondary to hypoxic encephalopathy was excluded from this study, so were recurrent SE episodes. The outcome measure was death during hospital stay.

2.2. Score calculations

STESS and mSTESS were calculated as proposed by their developers [5,7]. Regarding EMSE, Leitinger et al. assessed models including six variables for their prognostic value in SE and found highest performance in a score including four domains: etiology (E; grouped into 15 categories), age (A; stratified in 10-year intervals), comorbidities (C), and EEG data (E) (=EMSE-EACE), while level of consciousness (L) and duration of SE (D) did not increase the diagnostic value of the models [8]. Recently, Pacha et al. evaluated an alternative version of EMSE including age, etiology, and level of consciousness (=EMSE-EAL) [14]. Because of partly incomplete data on comorbidities and/or EEG in our patients, we chose to apply EMSE-EAL in the present study. In patients with competing SE etiologies, the most severe one according to EMSE was considered for score calculations. Patients with underlying etiology not represented in EMSE were not assigned an EMSE-EAL score. In terms of the END-IT score, the item "Diazepam resistance" was replaced by "refractoriness to a first line of medication", particularly as 1) diazepam is not the benzodiazepine of first choice in the treatment of SE in our institution and 2) -despite generally accepted guidelines- not all patients receive a benzodiazepine as first SE treatment [15]. With regards to cerebral imaging, cerebral microangiopathy, amyloid angiopathy, and generalized atrophy were not interpreted as imaging lesions responsible for an SE episode. Patients without imaging data did not receive an END-IT score.

2.3. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 22.0 (http://www.spss.com), GraphPad Prism 7.0 (www.graphpad.com) and Medcalc 17.9.7 (www.medcalc.org). Two sided p values of less than 0.05 were considered statistically significant. For each analyzed score, a receiver operating characteristics (ROC) curve was generated. The resulting areas under the curves (AUCs) were then compared to assess score performances using the method by Hanley and McNeil [16]. The ROC curves were furthermore used to determine optimal cutoff values for in-hospital mortality via the Youden index. Based on the identified cutoff values, sensitivity, specificity, positive and negative predictive values (PPV, NPV), and the rate of correctly classified episodes were calculated for each score. Given controversial results in the current literature, for the STESS these calculations were performed for the cutoff points 3 and 4, regardless of which one was the identified optimal cutoff value. McNemar test was used to compare sensitivities, specificities, and the rates of correctly classified cases [17]. Only patients in whom the respective scores could be calculated were included into the pairwise statistical comparisons of two scoring tools.

Table 1
Overview of study cohort.

	Total cohort (n = 287)
Demographics	
Female gender	165 (57.5%)
Age on admission, y	71 (58–79)
Premorbid mRS	3 (1–4)
Status epilepticus characteristics	
Etiology	
Acute symptomatic	160 (55.7%)
Remote symptomatic	59 (20.6%)
Progressive symptomatic	42 (14.6%)
Unknown	26 (9.1%)
History of seizures	156 (54.4%)
Encephalitis	21 (7.3%)
Worst seizure type before initiation of treatment	
Simple partial or complex partial	135 (47.0%)
Generalized convulsive	131 (45.6%)
NCSE in coma	21 (7.3%)
Neuroradiological data	
Cerebral imaging findings available	253 (88.2%)
Treatment	
Tracheal intubation	90 (31.4%)
Refractoriness to 1st and 2nd line treatment	112 (39.0%)
Outcome	
In-hospital mortality	34 (11.8%)

Values are n (%) or median (interquartile range). Abbreviations: mRS, modified Rankin Scale; NCSE, Nonconvulsive Status Epilepticus in Coma.

3. Results

3.1. Study cohort

We identified 362 SE episodes in our databases in the 8 year period from 2007 to 2014. After exclusion of recurrent episodes, 287 cases remained for final analysis. Table 1 and Fig. 1 give an overview of the patient cohort. Data on age, premorbid modified Rankin Scale (mRS) score, underlying SE etiology, and history of previous seizures were complete, thus all patients could be given STESS and mSTESS scores. In 16/287 (5.6%) episodes, the underlying SE etiology was not represented in the EMSE. This concerned patients with SE provoked by systemic infection (n = 9), patients suffering from progressive neurodegenerative disease (n = 5), and SE associated with application of contrast agents or chemotherapy (n = 2). These patients could therefore not be assigned EMSE-EAL scores. A total of 34/287 (11.8%) patients lacked imaging data in our electronic database because they either did not receive imaging or because it was performed in another hospital before patients were transferred to our institution. Therefore, the END-IT score could only be calculated in the remaining 253 patients. Of those 101/253 (39.9%) received MRI imaging and the remaining 152/253 (60.1%) CT. 29/287 (10.1%) patients were not administered a benzodiazepine as the first line of therapy. In most of these cases (n = 17) the first AED applied was levetiracetam, and a few patients received phenytoin, valproic acid, lacosamide, or anesthetic AEDs as first-line therapy.

3.2. Comparison of AUCs for prediction of in-hospital mortality

The statistical comparison of STESS and mSTESS included all patients (n = 287), while comparison of EMSE-EAL and END-IT with STESS and mSTESS was performed in the subset of patients with available EMSE-EAL (n = 271) and END-IT scores (n = 253) respectively. The comparison of EMSE-EAL with END-IT included patients with available scores for those two scoring tools (n = 240). The ROC curves for the prediction of in-hospital mortality are depicted in Fig. 2. AUCs were similar for STESS (0.628; 95% CI, 0.529–0.727), mSTESS (0.620; 95% CI, 0.510–0.731), END-IT (0.659; 95% CI, 0.550–