Seizure 56 (2018) 98–103

Contents lists available at ScienceDirect

Seizure

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

Refractory status epilepticus: Impact of baseline comorbidity and usefulness of STESS and EMSE scoring systems in predicting mortality and functional outcome

Jordi Ciurans*, Laia Grau-López, Marta Jiménez, Alejandra Fumanal, Maite Misis, Juan Luis Becerra

Department of Neurosciences, Hospital Germans Trias i Pujol, Universitat Autònoma de Barcelona C/Canyet s/n, 08916 Badalona, Spain

ARTICLE INFO

Article history:
Received 1 December 2017
Received in revised form 19 January 2018
Accepted 10 February 2018
Available online xxx

Keywords:
Refractory status epilepticus
STESS
EMSE
Outcome

ABSTRACT

Purpose: Little has been published on the prognostic value of the Status Epilepticus Severity Score (STESS) or the Epidemiology-based Mortality score in Status Epilepticus (EMSE) in refractory status epilepticus (RSE). We sought to analyze the prognostic value of STESS and EMSE and the impact of baseline comorbidities in mortality and functional outcome in RSE.

Methods: We designed an observational retrospective study of patients diagnosed with RSE between August 2013 and September 2017. For each patient, we analyzed prospectively recorded demographic, clinical, comorbidity, electroencephalographic, treatment, and hospital stay–related data and calculated STESS and EMSE. All variables were compared statistically between patients with good and poor functional outcome at discharge and between patients who died in hospital and those who were alive at discharge.

Results: Fourty-nine patients had RSE; 35.4% died in hospital and 88% showed functional decline at discharge. Mortality was associated with baseline chronic kidney disease (CKD) (OR 19.25, p = 0.006), baseline modified Rankin scale score (mRS) (OR 3.38, p = 0.005), non-convulsive status epilepticus (NCSE) with coma (OR 11.9, p = 0.04), STESS (OR 2, p = 0.04), and EMSE (OR 1.3, p = 0.02). Functional outcome was associated with baseline mRS (OR 13.9, p = 0.02), and EMSE (OR 1.3, p = 0.02). The optimal cutoff scores for predicting mortality were 4 for STESS and 60 for EMSE. EMSE predicted functional outcome with an optimal cutoff of 40.

Conclusions: CKD, NCSE with coma and STESS were associated with mortality. mRS and EMSE were associated with mortality and functional outcome. EMSE was useful for predicting functional outcome, while EMSE and STESS were useful for predicting in-hospital mortality.

1. Introduction

Refractory status epilepticus (RSE) is a life-threatening condition in which seizures do not respond to first and second-line antiepileptic drugs (AEDs) [1]. It usually requires the addition of a sedative drug. Super-refractory status epilepticus (SRSE) defines status epilepticus (SE) continuing after general anesthesia. RSE and SRSE are associated with severe systemic complications (cardiac arrhythmias, pneumonia, hypotension) [2] and high mortality, with rates of between 11.1% and 30% for RSE and 22%–50% for SRSE according to recent series [3–9]. Numerous factors have been associated with mortality and poor functional outcome in RSE, including age, etiology, acute symptomatic seizures, number of complications, cardiac and pulmonary complications, and seizure duration [10–18]. Associations with other comorbidities, such as chronic kidney disease (CKD), chronic liver disease, congestive heart failure, diabetes mellitus, chronic obstructive pulmonary disease, and oncologic disease have not yet been studied.

Two clinical scoring systems for predicting mortality in SE were recently introduced: STESS (Status Epilepticus Severity Score), which has four clinical components (level of consciousness, worst seizure type, age, and history of seizures) [19], and EMSE (Epidemiology-based Mortality score in Status Epilepticus), which also has four components (etiology, comorbidity, age, and electroencephalography [EEG]). The Charlson Comorbidity Index (CCI) takes morbidity into account and it is part of EMSE [20]. STESS ≥ 3 [19,21] and ≥ 4 [22,23] have been associated with

* Corresponding author.
E-mail address: jciurans.germanstrias@gencat.cat (J. Ciurans).

https://doi.org/10.1016/j.seizure.2018.02.007
1059-1311/

mortality while EMSE ≥ 64 [24] has been described as a good predictor of both mortality and morbidity in SE.

Few studies have analyzed the ability of STESS or EMSE to predict mortality and functional outcome in RSE. Madzar et al. [14] indicated that STESS ≥ 3 was a potential predictor of long-term functional outcome in this setting, while Gaspard et al. [18] reported that STESS was associated with both mortality and poor functional outcome in patients with new-onset RSE. The prognostic value of EMSE has not been studied in RSE.

The aims of this study were to evaluate the association between demographic, clinical, comorbidity, and therapeutic data and functional outcome and mortality in RSE and to investigate the prognostic value of STESS and EMSE in this setting.

2. Methods

2.1. Patients

This was an observational retrospective study of consecutive patients diagnosed with RSE at Hospital Germans Trias i Pujol, a tertiary hospital in Barcelona, Spain, between August 2013 and September 2017. Patients aged 16 years or younger and patients with anoxic-ischemic SE were excluded. The study variables analyzed had been systematically entered into a prospectively managed database according to an established protocol. The study was approved by the local ethics committee.

SE was defined according the Report of the ILAE Task Force on Classification of Status Epilepticus as a condition resulting in either from the failure of the mechanisms responsible for seizure termination or from the mechanisms which lead to prolonged seizures. Nonconvulsive status epilepticus (NCSE) was defined as a continuous nonconvulsive seizure that lasts >30 min, or multiple nonconvulsive seizures during a period of >30 min and between which sensory, motor and/or cognitive function is not fully recovered [25]. According to ILAE Task Force on Classification of SE we classified NCSE in NCSE with coma and NCSE without coma. The last includes generalized NCSE (typical, atypical, myoclonic absence), focal without impairment of consciousness, aphasic status, focal with impairment of consciousness and autonomic SE [26]. RSE was defined as a SE who failed to respond to the administration of at least one first-line agent (benzodiazepine) and failed to respond to at least one second-line agent (phenytoin, valproate, levetiracetam, lacosamide or other urgent control AED). The time limit to consider that SE did not respond to AED was 30 min for convulsive SE and 60 min for non convulsive SE [27]. Patients were admitted in the intensive care unit and the third line agents were administered when convulsions or alteration of level of consciousness persisted despite first and second line of treatment. Third line agents are defined as continuous intravenous infusions of midazolam, propofol, and thiopental at maintenance doses alone or in combination sufficient to produce a burst suppression pattern on the EEG. Patients were daily monitored with a video EEG for at least two hours. The EEG monitoring was stopped 24 h after the third line agents were retired. In our hospital, patients with CPSE younger than 65 years old with a level of consciousness that was not in a coma or stupor were not admitted to the intensive care unit (ICU) and they were not routinely treated with anesthetics. These patients were optimized using FAES by combining two, three or four second line drugs if necessary. These patients only entered in the intensive care unit when there was a medical complication that required orotracheal intubation or when the CPSE lasted more than 48–72 h.

The following variables were collected for all patients: age and gender; premorbid functional status measured using the modified Rankin Scale (mRS) and the Glasgow Outcome Scale (GOS), with a score of 1–3 indicating poor outcome and a score of 4–5 indicating good outcome [28]; presence, at the time of RSE diagnosis, of vascular disease (cerebrovascular disease, peripheral arterial disease, or ischemic heart disease), CKD (defined as kidney damage or a glomerular filtration rate [GFR] < 60 mL/min/1,73 m^2 for ≥3 months, according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Guidelines [29]), congestive heart failure (according to the European Cardiology Society [30]), diabetes mellitus, and cancer; the CCI; a history of previous epilepsy or SE; level of consciousness at diagnosis (alert or somnolent versus stuporous or comatose); seizure type according to the STESS scoring system (simple-partial, complex-partial, generalized convulsive, or non-convulsive in coma); type of SE according to the most recent International League Against Epilepsy classification [26], summarized as generalized convulsive, focal convulsive, nonconvulsive SE (NCSE) without coma, and NCSE with coma; etiology (symptomatic or cryptogenic, depending on whether or not a cause was identified during follow-up: pharmacological transgression, cerebrovascular disease, brain tumor, central nervous system infection, traumatic brain injury, alcohol withdrawal, metabolic alterations); EEG findings according to the EMSE scoring system (spontaneous burst suppression, after SE ictal discharges, generalized periodic discharges, lateralized periodic discharges, none of these); number of AEDs used and need for sedative drugs; SE duration (days); and length of stay in intensity care unit (ICU) and in hospital (days).

Functional outcome at discharge was assessed using the GOS. We consider as a worsening of the functional status the increase of one point or more of the GOS. In-hospital deaths were also recorded.

STESS and EMSE scores were calculated for all patients. STESS was calculated as follows: seizure type at presentation (simple partial, complex partial, or absence of seizures = 0 points, generalized convulsive seizure = 1 point, NCSE in coma = 2 points); history of seizures (yes = 0 points; no = 1 point), (age ≥ 65 years = 2 points; age < 65 years = 0 points), and level of consciousness at onset of SE (awake or somnolent = 0 points; stuporous or comatose = 1 point). EMSE scores were assessed as follows: etiology (central nervous system [CNS] anomalies [2 points], drug reduction/withdrawal/poor compliance [2 points], multiple sclerosis [5 points], remote cerebrovascular disease/brain injury [7 points], hydrocephalus [8 points], alcohol abuse [10 points], drug overdose [11 points], head trauma [12 points], cryptogenic [12 points], brain tumor [16 points], metabolic (sodium imbalance) [17 points], metabolic disorders [22 points], acute cerebrovascular disease [26 points], acute CNS infection [33 points], anoxia [65 points]); comorbidity (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, and diabetes [10 points each], hemiplegia, moderate or severe renal disease, diabetes with end organ damage, any tumor including leukemia/lymphoma [20 points each], moderate or severe liver disease [30 points], and metastatic solid tumor and AIDS [60 points each]); age (21–30 [1 point], 31–40 [2 points], 41–50 [3 points], 51–60 [5 points], 61–70 [7 points], 71–80 [points], and >80 [10 points]); and EEG patterns (spontaneous burst suppression [60 points], after SE ictal discharges [40 points], lateralized periodic discharges [40 points], generalized periodic discharges [40 points] and absence of the last three patterns [0 points]). The above disaggregated EMSE parameters were added as described in the original article by Leitinger et al. [20].

2.2. Statistical analysis

All variables were compared statistically between patients with good and poor functional outcome at discharge and between