# Convulsive Status Epilepticus in Indonesia

Machlusil Husna[1], Siti Nurlaela[2], Benny Arie Pradana[1], Firda Aushi[1], Priyo Atdisuramad[1]

[1]Department of Neurology, Faculty of Medicine Universitas Brawijaya - Saiful Anwar General Hospital, Malang, East Java Province, Indonesia
[2]Department of Neurology, Hermina Tangkuban Perahu General Hospital, Malang, East Java Province, Indonesia

Status epilepticus (SE) is a neurological emergency that is associated with significant mortality and morbidity. SE is classified as convulsive status epilepticus (CSE) when accompanied by motor contractions.[1] In adults, acute stroke is the most frequent etiology of SE. The other causes are metabolic disorders, hypoxia, and low levels of antiseizure medications.[2,3] The fatality rate of SE worldwide varies from 7% to 39%, and it is influenced by age, seizure duration, management, complications, and SE etiology.[4] In this study, we aimed to investigate the clinical characteristics, causes, and treatment outcomes of patients with CSE. We conducted a retrospective descriptive study using the data from the medical records of patients with CSE (age, ≥ 14 years) who were admitted to Saiful Anwar General Hospital in Malang, East Java Province, Indonesia, between January 1, 2010 and December 31, 2021. The patients were treated according to the SE management guidelines issued by the Indonesian Neurology Association, with some modifications due to limited drug availability.

The clinical characteristics of the 309 patients were analyzed (Table 1). The average age of the patients was 44.43 ± 17.6 years, and 32% of the patients were older than 50 years. The incidence of CSE was slightly more in males than in females (male:female ratio, 1.03:1). CSE was further classified into following three subgroups: focal (n = 34, 11%), focal to bilateral (n = 109, 35%), and generalized (n = 166, 54%). Most patients (n = 196, 63%) presented for treatment > 6 h after seizure onset. Brain imaging study was performed in 215 patients to evaluate suspected structural lesions, focal neurological deficits, uncontrolled seizures, or new-onset seizures in patients without a history of epilepsy. Stroke (n = 93, 43.2%) was the most common structural abnormality identified. Other abnormal findings included brain infections (n = 56, 26%), head trauma (n = 17, 7.9%), and brain tumors (n = 25, 11.6%). A total of 87 (28%) patients had a previous history of epilepsy. Other identifiable causes of CSE were antiseizure medication withdrawal (n = 41, 13.2%), hyperglycemia

(n = 10, 3.2%), uremic encephalopathy (n = 10, 3.2%), and septic encephalopathy (n = 9, 3%). EEG abnormalities were identified in 112 (42%) of the 261 patients who underwent the procedure. The most frequently observed abnormality in the EEGs was epileptiform discharge (n = 61, 54.4%). The epileptiform discharges were further categorized according to their morphology as follows: spike or sharp waves (n = 57, 93%), spike and wave (n = 3, 5%), and slow spike and wave (n = 1, 2%). Background activity, which reflects the overall electrical activity of the brain, also exhibited abnormalities in 50 patients (44.6%). An asymmetrical pattern was found in one patient (1%). Among the 309 patients who were administered diazepam, 48 (15.5%) experienced immediate seizure termination upon arrival at the hospital. Of the 223 patients treated with phenytoin, 192 (86.1%) had a positive response. A total of 23 patients (7.4%) with CSE required admission to the intensive care unit (ICU) for close monitoring and intensive management. All the patients with CSE in the ICU were administered midazolam for seizure control. Seven of these patients (2%) required mechanical ventilation for respiratory support, and four (1%) died. Among the patients who survived, seizure control was achieved in 19 (6%). The specific medications used in the patients are listed in Figure 1. During the study, 73 patients (24%) died, while 222 patients (72%) survived. The surviving patients were discharged after seizure control, which was achieved within 7 days. Septic shock was the most common cause of death (n = 26, 8.4%). The outcomes of the remaining 14 patients (4%) were unknown because they were transferred to another institution or were discharged against medical advice.

The average age of the patients with CSE in Indonesia (44.43 years) is lower than that of patients in Europe (69 years) and the United States (60 years).[5,6] In our study, the incidence of CSE was higher in men than in women, which is consistent with the findings of previous studies (men vs. women, 41.7/100,000 vs. 12.3/100,000).[7] A tonic-

**TABLE 1.** Characteristics of the Patients with CSE.

| Characteristics | Total (n) | Percentage (%) |
|---|---|---|
| **Age, years** | | |
| < 20 | 56 | 18 |
| 20-30 | 36 | 12 |
| 31-40 | 59 | 19 |
| 41-50 | 58 | 19 |
| > 50 | 100 | 32 |
| **Sex** | | |
| Male | 157 | 51 |
| Female | 152 | 49 |
| **Type of CSE** | | |
| Focal | 34 | 11 |
| Focal to bilateral | 109 | 35 |
| Generalized | 166 | 54 |
| **Time to treatment, h** | | |
| < 2 | 11 | 4 |
| 2-4 | 24 | 8 |
| 4-6 | 43 | 14 |
| > 6 | 196 | 63 |
| Unidentified | 35 | 11 |
| **History of preexisting epilepsy** | | |
| Yes | 87 | 28 |
| No | 214 | 69 |
| Unidentified | 8 | 3 |
| **Brain imaging** | | |
| Yes | 215 | 70 |
| No | 94 | 30 |
| **Results of brain imaging** | | |
| Normal | 24 | 11 |
| Abnormal | 191 | 89 |
| **EEG recording** | | |
| Yes | 261 | 84 |
| No | 48 | 16 |
| **Results of EEG** | | |
| Normal | 149 | 57 |
| Abnormal | 112 | 43 |
| **Survival status** | | |
| Alive | 222 | 72 |
| Died | 73 | 24 |
| Unidentified (referred to another hospital or discharged against medical advice) | 14 | 4 |

CSE, convulsive status epilepticus; EEG, electroencephalography.

clonic seizure is defined as a convulsion with contractions of both extremities and a decrease in consciousness. The duration of CSE was longer in our study than in previous studies conducted within the United States (duration, 79 min).[8] In our study, epileptiform discharges were mostly identified in patients with a stroke. This finding yielded a lower prevalence in a previous study that observed epileptiform discharges in 58 patients (44.27%).[9] In patients with ischemic stroke, the seizures may be caused by the disruption of the thalamocortical circuit due to the release of glutamate from the terminal axons. In hemorrhagic stroke, epileptogenesis involves the deposition of iron that inhibits several functions, including glutamate retrieval and glutamate synthetase functions.[10] The abnormal background rhythms on EEG indicate that patients with SE might suffer from encephalopathy-related complications, partly due to seizure-induced brain hypoxia or underlying brain diseases.[11] In our study, the EEG was normal in 57% of the patients with CSE. However, EEG could only be performed in 84% of the study patients, and the interictal recording time was only 30 min. Diazepam injection was the initial and subsequent therapy for seizure termination, as recommended by previous studies.[12] Due to limitations in intravenous access and resource availability, lorazepam was not readily available for use in this study. Phenytoin injection was chosen as the second-line drug due to its established efficacy and wider availability.[13] It successfully controlled the seizures in 86% of the patients with CSE. Midazolam infusion, known for its lower risk of respiratory complications, was chosen for refractory SE.[14] It successfully controlled seizures in 82.6% of these patients. The fatality rate in our study was 23.6% (n = 73). Septic shock was the most common cause of death (n = 26, 35.6%), which is consistent with the findings of previous studies. The most common cause of death in SE is its subsequent complications.[15] The higher fatality rate may be attributed to the longer duration of CSE observed in our study. However, the retrospective nature of our analysis limited our ability to establish a definitive cause-effect relationship between the fatality rate and CSE duration. Additionally, the study focused solely on patients with CSE, and limitations in our facilities prevented the use of a 24-hour EEG to differentiate between CSE and non-CSE.

In conclusion, stroke appears to be the most common etiology of CSE in Indonesia. Furthermore, CSE was associated with a fatality rate, with septic shock being the most frequent cause of death. In this study, limitations in drug availability hindered the implementation of some SE management guidelines set by the Indonesian Neurology Association. Nonetheless, these necessary drug substitutions, particularly diazepam as the first-line medication, were effective in treating SE. Our study findings highlight the potential of alternative antiseizure medications, such as diazepam, for the treatment of patients with CSE in resource-limited settings. Such strategies could improve patient outcomes when drug availability is limited.
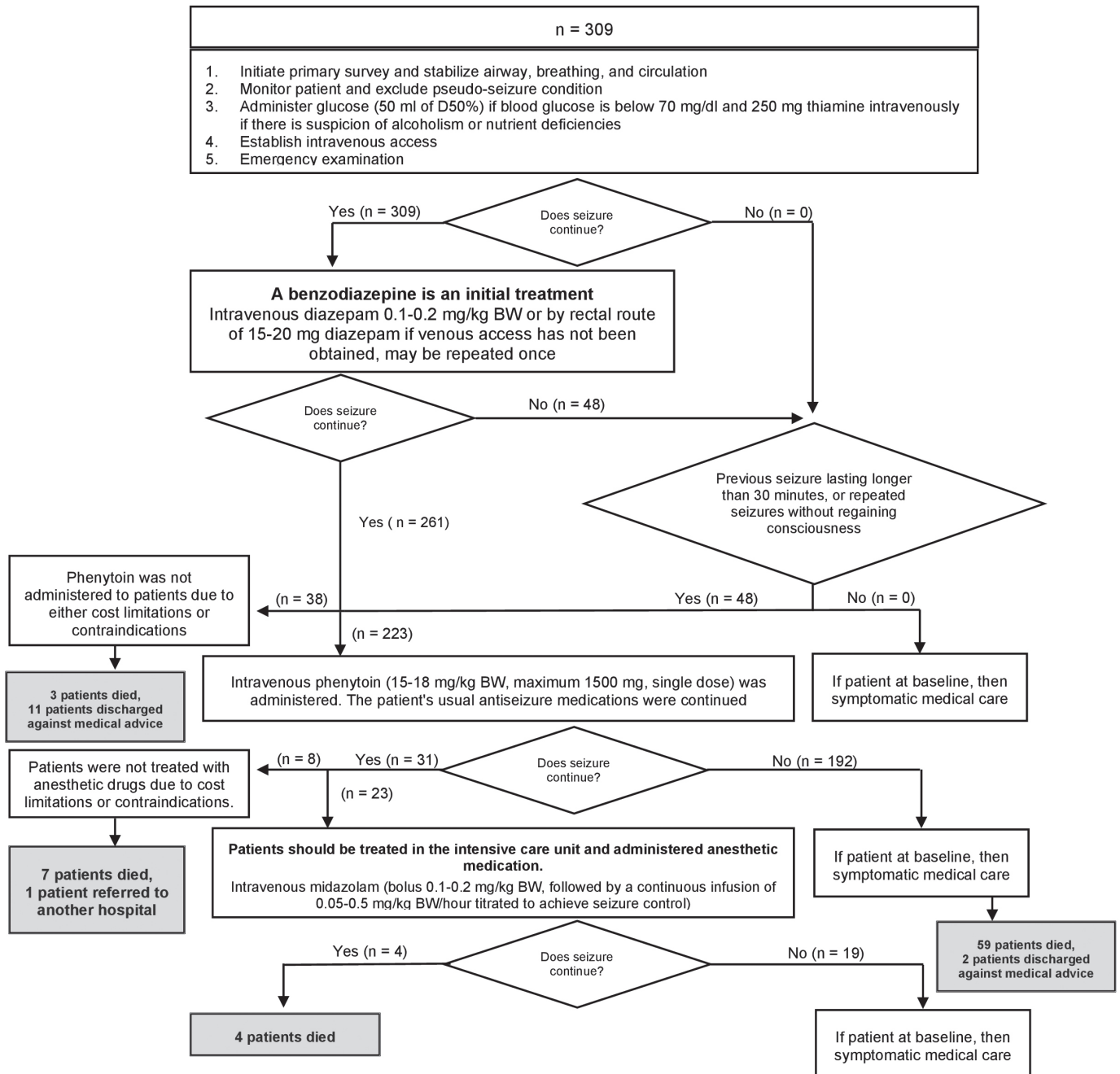
Husna et al. Convulsive Status Epilepticus in Indonesia

509



**FIG. 1.** Management of the patients with convulsive status epilepticus.

## REFERENCES

1. Ascoli M, Ferlazzo E, Gasparini S, et al. Epidemiology and Outcomes of Status Epilepticus. *Int J Gen Med.* 2021;14:2965-2973. [CrossRef]

2. Kong WY, Marawar R. Acute symptomatic seizures and status epilepticus in older adults: A narrative review focusing on management and outcomes. *Front Neurol.* 2022;13:954986. [CrossRef]

3. Nilo A, Pauletto G, Lorenzut S, et al. Post-Stroke Status Epilepticus: Time of Occurrence May Be the Difference? *J Clin Med.* 2023;12:769. [CrossRef]

4. Trinka E, Rainer LJ, Granbichler CA, Zimmermann G, Leitinger M. Mortality, and life expectancy in Epilepsy and Status epilepticus-current trends and future aspects. *Front Epidemiol.* 2023;3:1081757. [CrossRef]

5. Lu M, Faure M, Bergamasco A, et al. Epidemiology of status epilepticus in the United States: A systematic review. *Epilepsy Behav.* 2020;112:107459. [CrossRef]

6. Leitinger M, Trinka E, Zimmermann G, Granbichler CA, Kobulashvili T, Siebert U. Epidemiology of status epilepticus in adults: Apples, pears, and oranges - A critical review. *Epilepsy Behav*. 2020;103(Pt A):106720. [CrossRef]

7. Govoni V, Fallica E, Monetti VC, et al. Incidence of status epilepticus in southern Europe: a population study in the health district of Ferrara, Italy. *Eur Neurol.* 2008;59:120-126. [CrossRef]

8. Jenssen S, Gracely EJ, Sperling MR. How long do most seizures last? A systematic comparison of seizures recorded in the epilepsy monitoring unit. *Epilepsia.* 2006;47:1499-1503. [CrossRef]

9. Lasek-Bal A, Dewerenda-Sikora M, Binek Ł, et al. Epileptiform activity in the acute phase of stroke predicts the outcomes in patients without seizures. *Front Neurol.* 2023;14:1096876. [CrossRef]

10. Nicolo JP, O'Brien TJ, Kwan P. Role of cerebral glutamate in post-stroke epileptogenesis. Neuroimage Clin. 2019;24:102069. [CrossRef]

11. Britton JW, Frey LC, Hopp JL, et al. Electroencephalography (EEG): An Introductory Text and Atlas of Normal and Abnormal Findings in Adults, Children, and Infants [Internet]. St. Louis EK, Frey LC, editors. Chicago: American Epilepsy Society; 2016. [CrossRef]

12. Kienitz R, Kay L, Beuchat I, et al. Benzodiazepines in the Management of Seizures and Status Epilepticus: A Review of Routes of Delivery, Pharmacokinetics, Efficacy, and Tolerability. *CNS Drugs.* 2022;36:951-975. [CrossRef]

13. Nakamura K, Ohbe H, Matsui H, et al. Phenytoin versus fosphenytoin for second-line treatment of status epilepticus: propensity score matching analysis using a nationwide inpatient database. *Seizure.* 2020;80:124-130. [CrossRef]

14. Fernandez A, Lantigua H, Lesch C, et al. High-dose midazolam infusion for refractory status epilepticus. *Neurology.* 2014;82:359-365. [CrossRef]

15. Sirikarn P, Pattanittum P, Sawanyawisuth K, Tiamkao S. Causes of death in patients with status epilepticus. *Epilepsy Behav*. 2019;101:106372. [CrossRef]