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Extended Glasgow Outcome Scale in patients with moderate to severe traumatic brain injury experiencing non-convulsive status epilepticus

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ABSTRACT

Background and objectives. The severity of traumatic brain injury (TBI) is strongly linked to patient outcomes, with moderate to severe TBI associated with a high mortality rate. Similarly, non-convulsive status epilepticus (NCSE) also increases mortality. Patients with TBI have a higher risk of developing NCSE. However, the relationship between NCSE and patient outcomes remains poorly studied. This study will evaluate the association between NCSE and outcomes in patients with moderate to severe TBI using the Extended Glasgow Outcome Scale (GOSE).

Materials and methods. This retrospective study utilized data extracted from the medical records of adult patients (aged 18 and above) diagnosed with moderate to severe TBI at Rumah Sakit Umum Pusat Nasional Dr Cipto Mangunkusumo (RSCM) between March 2022 and February 2024. The third-month outcomes of these patients were assessed using the Extended Glasgow Outcome Scale (GOSE) and categorized as either good or bad based on whether the patients experienced NCSE as a complication of TBI.

Results. A total of 19 patients were included in this study, of which 13 (68%) were diagnosed with NCSE. Patients mainly were aged 18 to 24 (26%), male (47%), with motor vehicle accidents as the mechanism of injury (58%). Bad outcomes were slightly more common in patients with NCSE (70%) than those without NCSE (67%).

Conclusion. Non-convulsive status epilepticus in patients with moderate to severe TBI does not appear to have a significant association with poor outcomes, as measured by the GOSE when compared to patients without NCSE in this study. Although there is a slight difference in outcomes, this difference is not statistically significant.

Keywords: traumatic brain injury, non-convulsive status epilepticus, Extended Glasgow Outcome Scale, neurological outcomes, post-traumatic complications

Abbreviations:

TBI: Traumatic Brain Injury

NCSE: Non-Convulsive Status Epilepticus

GOSE: Extended Glasgow Outcome Scale

EEG: Electroencephalography

RSCM: Rumah Sakit Umum Pusat Nasional Dr. Cipto Mangunkusumo

AED: Anti-Epileptic Drug

GCS: Glasgow Coma Scale

ISS: Injury Severity Scale

M-TBI: Mild Traumatic Brain Injury

Mod-TBI: Moderate Traumatic Brain Injury

S-TBI: Severe Traumatic Brain Injury

Mod-S-TBI: Moderate to Severe Traumatic Brain Injury

PTS: Post-Traumatic Seizure

AED: Anti-Epileptic Drug

INTRODUCTION

Traumatic brain injury (TBI) refers to a temporary or permanent disorder of neurological functions affecting physical, cognitive, or psychosocial aspects caused by a mechanical trauma in brain tissue directly or indirectly and not a degenerative or congenital process [1]. Every year, it is estimated that 69 million people suffer from TBI, with the most cases in Africa and Southeast Asia (56%) and the lowest in North America (25%), with the most common causes being traffic accidents [2].

Patients who experience TBI can be classified into mild (M-TBI), moderate (Mod-TBI), or severe (S-TBI) depending on several parameters: Glasgow coma scale (GCS), duration of loss of consciousness, duration of posttraumatic amnesia, and the presence of focal neurological deficit event (Table 1.1) [3]. The patient's outcomes generally depend on this TBI severity. Respectively, the mortality of patients based on whether the TBI is mild, moderate, or severe is 0.1%, 10%, and 40% [2].

Table 1. TBI severity[3]

Category	GCS	Duration of Loss of Consciousness	Duration of Posttraumatic Amnesia	Presence of focal neurological deficit
Mild	13-15	<30 minutes	<1 day	None

Moderate	9-12	30 minutes - 24 hours	>1-7 days	Present/None
Severe	3-8	>24 hours	>7 days	Present/None

Seizure is a potential complication that can arise due to TBI. The prevalence of posttraumatic seizure (PTS) varies in the range of 2 to more than 50% of cases, with the highest prevalence of PTS being penetration injuries in military situations [4, 5]. In developing countries, PTS events range from 200 per 100,000 population per year and most often occur in cases of mod-TBI and s-TBI (potential events in 5 years onset of 1.2% and 10%) [6]. A study found seizures that occurred in 22% of patients with moderate to severe TBI (Mod-S-TBI) in the first 2 weeks, dominated by non-convulsive seizures [7].

While PTS are a known complication of TBI, one of the most challenging forms of seizure to diagnose and manage is non-convulsive status epilepticus (NCSE). Unlike convulsive seizures, NCSE often goes unnoticed because it does not present with the obvious motor symptoms typically associated with seizures[8]. This makes NCSE particularly difficult to detect and frequently underdiagnosed as in patients with Mod-S-TBI. Early recognition and intervention are critical for improving patient prognosis, as undiagnosed NCSE can lead to significant morbidity and increased mortality in these patients.

Numerous studies reveal the relationship of mortality in people with critical illnesses accompanied by prolonged non-convulsive seizures, generally with mental status changes being the manifestation of NCSE [9, 10]. No literature explicitly describes the outcomes of TBI patients who experience NCSE. Using the Glasgow Outcome Scale-Extended (GOSE) measuring device, this study assesses the relationship of the functional outcome to Mod-S-TBI patients who experience NCSE.

MATERIALS AND METHODS

This study utilized data from all neurotrauma cases recorded by the Neurotrauma division of the Neurology Department at the Dr. Cipto Mangunkusumo National General Hospital (RSCM). All Mod-S-TBI patients from March 2022 to February 2024, aged 18 years and older, who had EEG data recorded within three months (90 days) of the onset, were included in this analysis. Patients were excluded from the study if they had a history of epilepsy before the onset of the traumatic event, were hemodynamically unstable upon admission, had a history of a 'frailty' diagnosis in previous treatment, or if any critical data were missing and could not be extracted from medical records or confirmed by the patient.

The diagnosis of NCSE in this study was determined based on EEG results issued by the Neuroepilepsy division at RSCM, generally following the Salzburg criteria. EEG data were analyzed by qualified neurophysiologists using standard EEG software, and NCSE was diagnosed

accordingly. Patients with a definitive or possible diagnosis of NCSE were classified as experiencing NCSE. In contrast, patients with normal or abnormal EEG results that did not meet the diagnostic criteria for NCSE were classified as not experiencing NCSE.

Patient outcomes were measured using the GOSE, which in this study were grouped into good and poor outcomes. Outcomes were classified as good outcomes if the GOSE score was above 4 (independent, not requiring assistance for activities of daily living), while poor outcomes were defined as a GOSE score below 4 (requiring assistance for activities of daily living up to death). The relationship between NCSE and outcomes in Mod-S-TBI patients was assessed using Fisher's exact test, with a p-value of <0.05 considered significant.

Data Availability: Due to hospital policy, patient-specific data will not be made publicly available. However, de-identified data and protocols used in the study will be available upon reasonable request to the corresponding author.

RESULTS

This study included 19 patients aged 18 to 64 (median age 26). Most patients were involved in motorcycle accidents (N = 16), while the remaining patients fell from a height (N = 3). Patients received treatment for a duration varied ranging from 2 to 66 days, and all patients showed an improvement in their GCS scores from admission to outpatient care.

Table 2. Patient characteristics according to the EEG results

		EEG Results		
		Non-NCSE	NCSE	Total
Age (year old)	18-24	3 16%	5 26%	8 42%
	25-34	2 11%	2 11%	4 21%
	35-44	1 5%	2 11%	3 16%
	45-54	0 0%	1 5%	1 5%
	55-64	0 0%	3 16%	3 16%
Gender	Woman	0 0%	4 21%	4 21%
	Man	6 32%	9 47%	15 79%

Mechanism of trauma	Motorcycle accident	5 26%	11 58%	16 84%
	Fell from a height	1 5%	2 11%	3 16%
TBI severity	Moderate	4 21%	11 58%	15 79%
	Severe	2 11%	2 11%	4 21%
Admision GCS	13-15	1 5%	5 26%	6 32%
	9-12	3 16%	6 32%	9 47%
	3-8	2 11%	2 11%	4 21%
Discharge GCS	13-15	6 32%	10 53%	16 84%
	9-12	0 0%	3 16%	3 16%
	3-8	0 0%	0 0%	0 0%
Injury Severity Scale	0-15	4 21%	11 58%	15 79%
	>=16	2 11%	2 11%	4 21%
Average Treatment Duration (days)		34	21	25

Patients who experienced NCSE were distributed across all age groups, genders, TBI severity levels, and injury severity scale (ISS) categories. NCSE was most commonly observed in male patients (47%), in the 18-24 age group (26%), among those with Mod-TBI (58%), and in patients with an ISS of less than 16 (58%) (Table 3.1).

Thirteen patients with Mod-S-TBI experienced NCSE, while six other patients were found to have non-NCSE EEG results, with other abnormal EEG in this group showing slow wave patterns. Of the thirteen patients who experienced NCSE, 9 (70%) had poor outcomes, while 4 (30%) had good outcomes, and the remaining patients without NCSE also had a high rate of poor

outcomes (67%). Statistical analysis did not indicate a significant association between NCSE and poor outcomes (OR 1.125, 95% CI: 0.143-8.880, p = 1.000).

Table 3. EEG results and GOSE outcomes

		Patient outcomes (GOSE)		
		Good	Poor	Total
EEG results	Non NCSE	2 (33%)	4 (67%)	6
	NCSE	4 (30%)	9 (70%)	13

DISCUSSION

The findings of this study highlight an important aspect of moderate to severe TBI, particularly the impact of NCSE on patient outcomes. While NCSE is often associated with increased morbidity and mortality in critically ill patients [9, 11], this study did not find a statistically significant difference in outcomes between patients with and without NCSE. Although the NCSE group showed a slightly higher proportion of poor outcomes (70% versus 67%), this difference is not significant and must be interpreted with caution due to the small sample size. Given the small sample, even a single additional patient in the non-NCSE group could potentially shift the proportion and alter the interpretation. Thus, while the trend toward poorer outcomes in the NCSE group is notable, it is not yet conclusive and warrants further investigation in larger studies.

This discrepancy could be attributed to the small sample size, which limits the study's statistical power and ability to detect subtle differences. Larger studies are needed to validate these findings and potentially identify factors that might modulate the relationship between NCSE and outcomes in TBI patients, such as the timing and effectiveness of interventions, the severity of NCSE, or variations in treatment protocols.

Limitations

Several factors may have contributed to the lack of statistical significance in this study. The retrospective design posed inherent limitations, as certain risk factors influencing patient outcomes—such as variations in clinical management, and differences in the timing, dosage, and type of anti-epileptic drug (AED) administration—could not be fully controlled. The data relied solely on the available documentation in the patient's medical records, which may not have captured all relevant clinical variables. While AEDs were generally administered to patients, the variation in treatment regimens further complicated the data analysis and potentially affected the consistency of patient outcomes. Additionally, the small sample size reduced the study's statistical power, limiting its ability to detect subtle differences between groups. Finally, some dependent variable

data were recorded after a period when this study was conducted, based on anamnesis obtained from patients or their families due to missing data or the need for confirmation. This may have introduced recall bias.

Another limitation of this study is related to the use of the GOSE to assess patient outcomes. While the GOSE is widely utilized for evaluating post-traumatic recovery, it remains a relatively subjective measure that relies on clinical assessments, which can be influenced by evaluator bias or variability in interpretation. Moreover, the GOSE primarily focuses on physical recovery, and may not fully capture the complex cognitive or psychological consequences of TBI, particularly in patients who experience NCSE, which may have subtle, long-term effects on cognitive function and mental health. This limitation may have led to an underestimation of the true impact of NCSE on overall recovery and quality of life for these patients.

Despite these limitations, the study's findings provide valuable insight into the impact of NCSE on Mod-S-TBI patients within the first three months following TBI onset. Early detection of NCSE remains crucial for patient care, as seizures, especially non-convulsive seizures, are known to significantly increase mortality rates. Therefore, timely and appropriate treatment is essential to improve outcomes.

This research serves as a foundation for future studies on the complications of NCSE in TBI patients. There are also opportunities for future research using more robust study design, such as a prospective cohort study with larger sample sizes. These studies could better identify additional risk factors, including the effectiveness of NCSE interventions in TBI patients. Furthermore, long-term follow-up studies on patients who experience NCSE could provide more comprehensive insights into the long-term impact of NCSE on patients' quality of life and their subsequent rehabilitation needs.

CONCLUSION

This study explored the occurrence of NCSE in patients with Mod-S-TBI. While NCSE is a recognized complication of TBI, this study findings did not demonstrate a statistically significant difference in patient outcomes between those with and without NCSE. Despite a slightly higher proportion of poor outcomes in the NCSE group, the small sample size and the inherent limitations of the study's retrospective design may have contributed to the lack of statistical significance. Variations in clinical management, differences in anti-epileptic drug (AED) treatment protocols, and the reliance on patient anamnesis for some dependent variables could also have influenced the results.

Further research with larger sample sizes and prospective study designs is needed to confirm these findings and explore the impact of different treatment strategies for NCSE in TBI patients. Additionally, the role of early intervention and the effectiveness of AEDs in modulating

long-term outcomes should be considered in future studies to better understand the relationship between NCSE and TBI prognosis.

Conflict of interest:

The authors declare that they have no financial interest or any conflict of interest related to the publication of this article.

Author's contributions:

Conceptualization, methodology, writing – original draft, writing – review & editing, A.D.B.; supervision, Y.R. and R.A.Z.

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FIGURES, TABLES AND SCHEMES

TABLES

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