

# Usefulness of Modified Cave Score to Identify Seizure in Adult Patients with Intracerebral Hemorrhage in Emergency Room

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## Abstract

**Introduction:** Seizure is a common neurological disorder causing physical, psychological, emotional, social, and economic effects. Seizure is a serious complication of spontaneous intracerebral hemorrhage (ICH), which can cause significant disability and mortality. The purpose of the study is to determine the frequency of post-ICH seizure, possible associated factors, and use the modified CAVE score (CAVE2) to identify seizures (mainly late seizures) and assess outcomes in terms of mortality at Devdaha Medical College and Research Institute (DMCRI), Nepal.

**Methods:** This was a descriptive cross-sectional hospital-based study conducted among adult patients attending the emergency room of DMCRI from January 2025 to June 2025 over a six-month period. The study commenced after obtaining ethical approval from the Institutional Review Committee (Reference No: 21/2024). The inclusion criteria consisted of adult patients aged 18 years or above with ICH bleed diagnosed based on history, examination, and CT head, and admitted for complete neurological intervention. Collected data was collected using structured questionnaires, and analysis was performed by using Microsoft Excel and SPSS V.21. C-statistics (ROC) were calculated, and a 95 % confidence interval was taken.

**Results:** A total of 73 cases between 18 and 86 years of ICH were included. 43 (59%) were male, and 30 (41%) were female. Mean duration of Hospital stay was 17 days (SD±3.74) with a maximum of 47 days and a minimum of 9 days. Late seizure was developed in 14 patients (19.17%), whereas early seizure was in 8 (10.9%) patients. Late seizure was 100% in a hypertensive patient with ICH bleed, followed by a smoker (92.8%) and an alcohol consumer (85.7%). Calculated CAVE2 scores with seizure percentage: 0 (0%), 1(5.5%), 2(16.6%),3(25%),4(83.3%), and 5(100%). The calculated C-statistic (ROC) for the CAVE2 scores was 0.87. In the hospital, the mortality was (n=19, 26%).

**Conclusion:** The CAVE2 score can identify patients with a high risk of late seizures. The higher the score, the higher the risk of getting seizures in the future. CAVE 2 score in the emergency room helps to triage patients and guide treatment.

**Keywords:** Seizure, intra cerebral hemorrhage, Modified CAVE (CAVE2), emergency, outcomes

## Introduction

A seizure is a common neurological emergency that is defined as a paroxysmal motor, sensory, autonomic, or psychic event due to abnormal, excessive synchronous electrical discharges from the brain.<sup>1</sup> Seizures are common in patients with intracranial hemorrhage (ICH). Early seizures are defined as seizures that appear within 1 week, and late seizures appear after more than 1 week of ICH.<sup>2</sup> Common feature is that both early and late seizures are associated with a worse prognosis and poor clinical outcome, greater disability, and greater mortality.<sup>3,4,5</sup>

The symptomatic seizures among patients with ICH range between 5% and 14% within the first twenty-four hours of stroke.<sup>6</sup> Bleeding inside the cranium can be epidural, subdural, arachnoids, intra ventricular, or intra cerebral. Intra cerebral hemorrhage accounts for approximately 10 % to 20 % of all strokes.<sup>7</sup> In 2014, Haapaniemi et al. proposed the CAVE scale, having four parameters each carrying one score (C cortical involvement, A age of patient less than 65 years, V volume of hemorrhage more than 10mm, and E early onset seizure), for the prediction of post-hemorrhagic stroke seizure. The maximum score is 4, and a score of 2 or more is related to 81% sensitivity and 89% specificity for the occurrence of late seizure. The risk of post-stroke epilepsy was estimated at 0.6%, 3.6%, 9.8%, 34.8%, and 46.2%, corresponding to CAVE scores 0 to 4, respectively. The CAVE score seems to be an easy tool to apply. However, it only applies to hemorrhagic strokes, which limits its use.<sup>8</sup> Some studies show that cortex involvement increases the risk of seizures, when the cortex score was changed to 2 points, which increases the predicted value of the CAVE score. Thus, in 2023, the CAVE Score was refined into the Modified CAVE (CAVE 2) score using data from 408 patients in Taiwan. The CAVE2 score was proposed, which includes 2 points for cortex involvement and 1 point each for age <65, hematoma volume >10 ml, and early seizures.<sup>9</sup>

## Methods

This single-center study was conducted in the emergency room at DMC-RI, one of the major referral tertiary hospitals in western Nepal. The study population comprised adult patients aged 18 years and above who were diagnosed with ICH bleed during the six months of the study period, from January 2025 to June 2025. A total of 84 patients were admitted and treated for ICH; however, 11 patients were excluded as they did not fulfill the inclusion criteria. A total of N=73 patients were followed till their complete hospital stay and were enrolled in the study. The inclusion criteria were adult patients with new spontaneous intra cerebral bleed, whereas patients diagnosed as pseudo seizure, head injury, TIA, brain tumor, SAH, SDH, Ischemic stroke with hemorrhagic transformation, anticoagulant drugs, patients who did not provide consent, and patients below 18 years were excluded. Informed consent was obtained from willing participants. A non-probability convenience sampling

method was used, allowing the inclusion of all eligible cases that presented themselves within the stated timeframe. Data were collected using a structured questionnaire that included demographic characteristics. Modified CAVE (CAVE2) was calculated for each patient. Clinical records, CT head findings, and laboratory investigations were reviewed to supplement the patient interviews. Hematoma volume was calculated according to the  $A \times B \times C/2$  method.<sup>10</sup> Collected data was performed using structured questionnaires, and analysis was performed by using Microsoft Excel and SPSS V.21. C-Statistics (ROC) was calculated, and a 95 % confidence interval was taken.

Sampling method/technique: Quantitative, Non-probability convenience sampling

Sample Size: 73

Justification of sample size

$$n = Z^2 \times P \times (1 - P) / e^2$$

Z: for confidence interval of 95%, Z = 1.96

P = Prevalence

e = allowable error (6 %)

Prevalence in adults = 7.3 %.<sup>11, 12</sup>

Total sample size will be =  $1.96^2 \times 0.073 \times (1-0.073) / 0.0036 = 73$

(Modified CAVE / CAVE 2 ): Score

Variables	Point / score
C. Cortex involvement	2
A. age < 65 year	1
V. Volume > 10ml	1
E. Early seizure	1
Total CAVE 2 Score	5

Limitations like being single-center in nature may not allow wide generalizability, while reliance on convenience sampling may result in selection bias. Moreover, we only analyzed patients with motor seizures, which may underestimate the late seizure rate. The study excluded patients who lost follow-up after discharge from the hospital.

## Results

During the study period, 84 patients were admitted and treated for ICH; 11 patients were excluded as they did not fulfill the inclusion criteria. A total of 73 patients could be followed till hospital stay and enrolled in the study (Table 1). Proportions of males were 43 (59%) and females were 30 (41%). Late seizure was more than 21% in males, as females had 16.7%.

**Table 1:** Characteristics of patients: Late seizure was developed in 14 patients (19.17%), whereas early seizure was in 8 (10.9%) patients. Eight patients with an age of less than 65 had late seizure, while late seizure was developed in six patients with an age greater than 65.

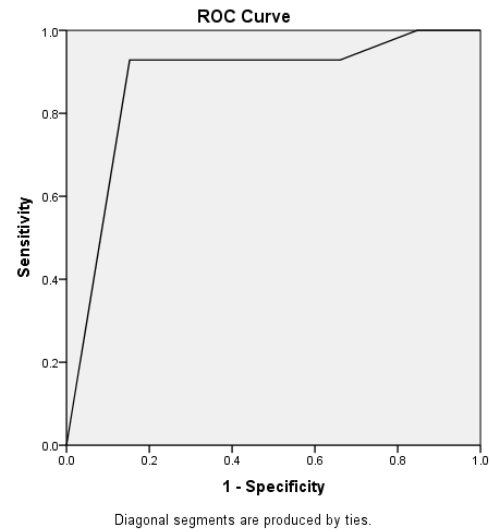
Variables (n=73)	No Seizure (n = 59)	Late Seizure (n= 14)
SEX		
Male (43)	34	9
Female (30)	25	5
AGE		
< 65 (39)	31	8
>= 65 (34)	28	6
CORTEX INVOLVEMENT		
Yes (19)	11	8
No (54)	48	6
VOLUME (ml)		
<= 10 CC (57)	52	5
>10 CC (16)	7	9
EARLY SEIZURE		
Yes (8)	5	3
No (65)	54	11

**Table 2:** Risk factors associated with ICH and late seizure: Co-morbidity of the patient was associated with late seizure. All patients 100% (n=14) with hypertension developed late seizure (n=14) followed by 192.8% (n=13) smokers and 85.7% (n=12) developed late seizure.

Variable	No Seizure (n = 59)	Late Seizure (n=14)	P Value
Hypertension (52)	38	14(100%)	< 0.001
Diabetes Mellitus (36)	27	9(64.2%)	< 0.001
Dyslipidemia (55)	46	9 (64.2%)	< 0.001
Smoker (45)	32	13(92.8%)	< 0.001
Alcohol consumer (52)	40	12 (85.7%)	< 0.001

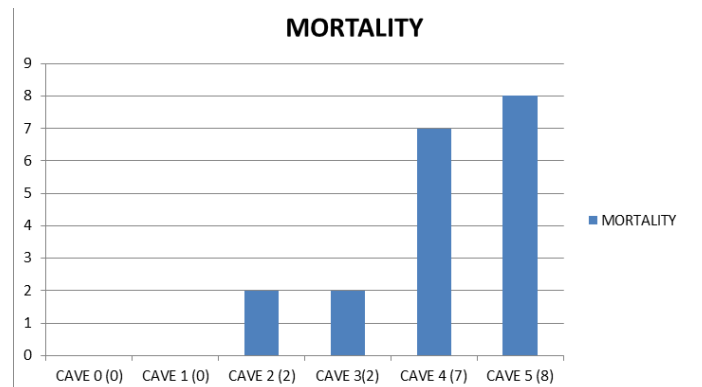
**Table 3:** Relations Modified CAVE (CAVE 2) score and late seizure: Risk of developing late seizure increases with an increase in CAVE 2 score. Late seizure was developed in all patients having a CAVE2 score range from 1 to 5; however, the patient with 0 CAVE2 had no seizure.

Score	Patient number (n=73)	No Seizure (n=59)	Late Seizure (n=14)
0	22	22	0 (0%)
1	18	17	1 (5.5%)
2	12	10	2 (16.66%)
3	12	9	3 (25%)
4	6	1	5 (83.3%)
5	3	0	3 (100%)



**Figure 1:** AUROC (Area under receiver operating curve) of CAVE 2 scores at 95% CI to identify predictive accuracy for late seizure: The calculated Concordance statistic / C-statistic (AUROC) was 0.825, which suggests good predictive ability of CAVE 2 scores to find the possibility of late seizure in ICH patients.

Area Under receiver Operating Curve ( AU ROC ) = 0.875				
Test Result Variable(s): Predicted probability				
Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.875	.055	.000	.767	.984



**Figure 2:** Mortality: Out of 73 patients, 19 died during treatment at the ICU, and the remaining had focal neurological deficits due to intracranial bleed. In hospital mortality according to the modified CAVE score, the highest mortality (n = 8) was in the CAVE 2 score, followed by 7 deaths in the CAVE 4 score. Cave scores of 0 and 1 have no mortality.

## Discussion

Spontaneous, non-traumatic intra cerebral hemorrhage (ICH) is the second most common type of stroke and is linked to high rates of death and lasting disability.<sup>13</sup>

In this study, late seizures occurred in 9 men (64.3%) and 5 women (35.7%). This male predominance matches the findings by Huang YC et al.<sup>9</sup>, who reported 41 men (15.1%) and 11 women (8.0%) with late seizures following intra cerebral hemorrhage. Whereas a study conducted by Ismail M et al.<sup>14</sup> had a higher proportion in females, 53.6% than males, 46.4 %. This gender variation may be due to biological and hormonal differences (men have larger amygdale/thalamus and women tend to have larger hippocampus and cortical regions, estrogen and progesterone affect recovering neural injury.<sup>15</sup> Similarly, men often experience ICH at younger ages, which may also contribute to higher seizure rates among younger males.<sup>16</sup>

### Incidence:

The incidence of late seizure in our study was 19.18 % which was higher than the study by Wang et al., being 11.1%.<sup>17</sup>, Huang YC et al.<sup>9</sup> being 12.7% and Haapaniemi et al.<sup>8</sup> being 9.2%, however, it lines with the study by H. Butzkueven et al.<sup>18</sup> being 19%. The variation in incidence across different hospitals may be due to the availability of diagnostic methods for additional autoimmune vascular disease, prior use of early anti seizure medication<sup>19</sup> and patient demography (younger patients are more likely to have late seizure).<sup>9</sup> Incidence of early seizure in our study was 10.95 %, which lines with the study by Haapaniemi et al.<sup>8</sup> being 11.0%. Whereas, a study by Ismail M et al.<sup>14</sup> shows 14.4 % had early seizure.

### Risk factor for seizure:

We found hypertension as a major risk factor in 14 (100%) patients for late seizure (n=14), followed by smoking in 13 (92.8%) and alcohol consumption in 12 (85.7%). A similar finding was found in research by Rossi et al.<sup>20</sup>, where hypertension was a risk factor in 16(52%) patients for late seizure (n=31), followed by smoking in 8 (26%) patients. However, multivariate analysis conducted by Wang et al.<sup>17</sup> and Ma S et al.<sup>21</sup> in China shows there was no relationship between seizure and risk factors for stroke (such as hypertension, diabetes mellitus, and coronary heart disease). This difference may be due to the low prevalence of risk factors in the sample population and study period context.

### Mortality:

A 26% mortality rate in ICH patients in our study is notably high but aligns with findings of a single-center study from Iran (mortality 36%).<sup>22</sup> However, in the Finnish study, post-stroke seizure patients experienced a relatively low mortality rate of 10.4%.<sup>8</sup> Variation in mortality across different

studies is likely due to Cortical involvement, Hemorrhagic transformation of an infarct, and Intra cerebral hemorrhage (ICH).<sup>21</sup> Also, Mortality among seizure patients may also vary depending on the availability of immediate emergency and intensive care services, urgency and success of neurosurgical interventions, patient characteristics such as age, sex, and co-morbidities, and timely use of antiepileptic medications.

The relation between the modified cave score (CAVE2) and late seizure:

We used CAVE2 (where cortical hemorrhage scores 2 points) to stratify risk of late seizure after ICH and found possibility of late seizure increases with increase in CAVE2 scores: 0 (0%), 1(5.5%), 2(16.6%),3(25%),4(83.3%)and 5(100%). Our Finding aligns with retrospective study by Huang YC et al.<sup>9</sup> in Taiwan, where the incidence of late seizures correlated with increasing CAVE2 scores: Score 0: 0%, Score 1: 4.6%, Score 2: 18.3%, Score  $\geq$ 3: 54.4%.

Our study reported a C-statistic (ROC) of 0.875 for CAVE2, indicating good predictive ability for late seizure. Similarly, the study reported by Huang YC et al.<sup>9</sup> had a C-statistic of 0.74, which also shows good predictive capability. A slightly higher C-statistic for identifying late seizure in our study may be due to limited Acute Stroke Care, delays in Intervention, larger and untreated cortical infarcts or hemorrhages, poor treatment in hypertension and diabetes.<sup>23</sup>

## Conclusion

The CAVE2 score can identify patients with a high risk of late seizures. The higher the score, the higher the risk of getting seizures in the future. For example, someone with a score of 3 or more has a more than 50% chance of late seizures. The CAVE2 score is a quick, easy tool used in the emergency room to identify ICH patients at high risk for later seizures, helping guide decisions on starting preventive anti-seizure medication and determining whether to admit to ICU or a high care unit.

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