

## Introduction

Cerebrovascular disease is a leading cause of acquired epilepsy. Potential risk factors implicated in predisposing for seizure include location and size of hemorrhage, patient age, and stroke severity. The role of prophylactic anticonvulsants in preventing seizures and/or improving outcome after intracerebral hemorrhage (ICH) remains controversial. Current guidelines recommend against prophylaxis. However, these recommendations are based on older studies primarily utilizing phenytoin (Dilantin) as the anticonvulsant of choice. Newer medications, such as levetiracetam (Keppra), have yet to be extensively studied. Here, we analyze the influence of AED prophylaxis on seizure incidence and outcome (discharge mRS & NIHSS score) after ICH.

## Methods

We performed a retrospective review of our clinical database from 2010 to 2015. All patients with the diagnosis of ICH and those without prior seizure diagnoses were included. Patients were divided into those who received prophylactic anticonvulsants and those who did not. Patient demographics, CT/MRI lesion parameters, as well as seizure data and outcomes were collected. Results were analyzed using binary logistic regression and quantile regression models, each analysis was corrected for age, gender, and initial NIHSS score.

## Learning Objectives

1) Describe the role of AED prophylaxis on seizure events and outcomes after intracerebral

## Results

A total of 522 patients were included in the study. Median pre-admission NIHSS was 10 (IQR, 2-19), prophylaxis group 12 (IQR, 4-23), and no prophylaxis group 6 (IQR, 1-18.5),  $p=0.003$ . Of the 342 patients (65.5%) that received prophylactic anticonvulsants, 320 (94%) received levetiracetam and 27 (7.9%) had seizure events compared with 22 (12.2%) of those without prophylaxis. Patients with prophylaxis treatment had significantly larger areas of hemorrhage; 10.0 mL (IQR, 4.1-21.3) compared to those without 4.8 mL (IQR, 1.4-13.7,  $p<0.001$ )

**Table 1. Baseline Characteristics**

Baseline Characteristics	No. (%) of Patients w/Seizure Prophylaxis (N=342)	No. (%) of Patients w/o Seizure Prophylaxis (N=180)	P value
Age, median (IQR), y	70 (58-80)	71 (62-81)	0.173
Men	185 (54.1)	92 (51.1)	0.520
Hypertension	274 (80.1)	138 (76.7)	0.368
Diabetes Mellitus	119 (34.8)	55 (30.6)	0.379
COPD	47 (13.7)	24 (13.3)	1.00
Alcohol Use	13 (3.8)	8 (4.4)	0.815
Tobacco use	52 (15.2)	27 (15.0)	1.00
Coronary Artery Disease	85 (24.9)	51 (28.3)	0.403
Seizure Event	27 (7.9)	22 (12.2)	0.116
Pre-admission NIH Stroke Scale Score (Median, IQR)	12.0 (12-35) (N=278)	6.0 (1-18.5) (N=138)	0.003
Discharge NIH Stroke Scale Score (Median, IQR)	12.0 (3.0-25) (N=280)	4.0 (1-18) (N=139)	0.001
Last mRS Result (Median, IQR)	1.0 (0-4) (N=158)	1.0 (0-3) (N=67)	0.991
Extension (Dural or Intraventricular)	153 (44.7)	68 (37.8)	0.119
Cortical Involvement	144 (42.1)	40 (22.2)	<0.001
Prior Infarct (lacunar or Territorial)	28 (8.2)	13 (7.2)	0.690
Size of Hemorrhage (mL) (Median, IQR)	10.0 (4.1-21.3) (N=296)	4.8 (1.4-13.7) (N=148)	<0.001
Favorable Outcome (mRS 0-2)	184 (53.8%)	113 (62.8)	0.130
Discharge to Home	100 (29.2)	55 (30.6)	0.763
Discharge to Home or Rehab	208 (60.8)	120 (66.7)	0.111
Total Hospital Cost (mean, STD)	\$76112 (\$86478)	\$47467 (\$59363)	<0.001

Treatment with anticonvulsant prophylaxis was associated with significantly lower odds of clinical seizure (adjusted OR, 0.44; 95% CI, 0.23-0.97) after correcting for initial NIHSS score, age, and sex.

**Table 2. Risk Factors**

Risk Factor	Patients with Seizure	Patients without seizure	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted P value
AED Prophylaxis (Yes vs No)					0.042
Yes	19 (6.8%)	259	0.62 (0.29, 1.22)	0.44 (0.20, 0.97)	
No	15 (10.8%)	123	1 [Reference]	1 [Reference]	
Sex (Female vs Male)					0.314
Female	19 (7.7%)	226	0.69 (0.38, 1.26)	0.68 (0.32, 1.4)	
Male	30 (10.8%)	247	1 [Reference]	1 [Reference]	
Age (Category vs <55 yrs)					0.008
<55	16 (14.6%)	79	1 [Reference]	1 [Reference]	
55-64	7 (16.8%)	130	1.18 (0.53, 2.6)	1.42 (0.53, 3.8)	
65-74	11 (5.1%)	118	0.32 (0.12, 0.82)	0.17 (0.04, 0.70)	
75-84	13 (8.5%)	76	0.55 (0.23, 1.3)	0.71 (0.26, 1.96)	
>85	2 (2.8%)	70	0.17 (0.04, 0.77)	0.12 (0.01, 0.98)	
Pre-admission NIHSS (Severity of Stroke vs No Stroke)					0.084
No Stroke Symptoms	3 (7.9%)	35	1 [Reference]	1 [Reference]	
Minor	9 (8.8%)	93	2.37 (0.91, 6.19)	1.08 (0.27, 4.39)	
Moderate	10 (8.8%)	104	3.58 (1.38, 9.33)	1.34 (0.33, 5.43)	
Mod - Severe	7 (16.2%)	36	3.77 (1.17, 12.17)	3.55 (0.77, 16.28)	
Severe	5 (4.2%)	114	1.62 (0.38, 6.89)	0.59 (0.13, 2.73)	

Younger patients treated with anticonvulsant prophylaxis were associated with an increase in seizure events (cat. 55-64 yrs; adjusted OR, 1.42 (0.53, 3.8). However, there were no significant differences in discharge NIHSS (difference, 0.0; 95% CI, -0.83, 0.83;  $p=1.00$ ) and discharge mRS (difference, 0.0; 95%CI, -0.0, 0.0;  $p=1.00$ ) between groups. Median length of stay was longer for those with prophylaxis (difference, 1.5 days; 95%CI, 2.4-0.6;  $p=0.001$ ) and total hospital costs were higher with prophylaxis (difference, 8441; 95% CI, 1667, 15125;  $p=0.015$ )

**Table 3: NIHSS Score Quantile Regression Analysis**

Risk Factor	Median NIHSS Score (IQR)	Difference (95% CI)	Adjusted Difference (95% CI)	Adjusted P Value
AED Prophylaxis (No vs Yes)				
Yes	12.0 (3.0, 25)	8.0 (-10.7, -5.3)	0.0 (-0.8, 0.8)	1.00
No	4.5 (1.0, 18.0)	Reference	Reference	
Sex (Male vs Female)				
Male	8.0 (-6.7, 2.7)	-2.0 (-6.7, 2.7)	-0.5 (-1.4, 0.40)	0.275
Female	10.5 (25.0, 2.0)	Reference	Reference	
Age (Category vs >85 yrs)				
<55	9.5 (2.0, 23.0)	Reference	Reference	
55-64	7.0 (1.0, 22.5)	-2.0 (-10.0, 6.0)	-0.5 (-1.8, 0.8)	0.45
65-74	11.0 (3.0, 26.0)	2.0 (-6.2, 10.2)	0.5 (-0.9, 1.9)	1.00
75-84	9.0 (2.0, 26.0)	0.0 (-7.4, 7.4)	0.5 (-1.6, 1.6)	0.50
>85	10.0 (2.0, 26.0)	1.0 (-6.9, 8.9)	0.0 (-1.8, 1.8)	1.00
Pre-admission NIHSS Score (Stroke Severity vs No Stroke)				
No stroke	0 (0, 1.0)	Reference	Reference	
Minor	2.0 (1.0, 4.0)	2.0 (1.0, 3.0)	1.5 (0.37, 2.7)	0.001
Moderate	7.0 (3.0, 12.0)	7.0 (5.2, 8.8)	7.0 (5.5, 8.5)	<0.001
Mod-Severe	16.5 (13.0, 22.0)	17.0 (15.3, 18.7)	16.5 (14.8, 18.2)	<0.001
Severe	31.0 (23.0, 38.0)	31.0 (29.0, 33.0)	31.0 (29.0, 33.0)	<0.001

## Conclusions

Stroke remains one of the most common causes of acquired epilepsy and few risk factors have been consistently predictive of seizure onset. Administration of predominantly levetiracetam for anticonvulsant prophylaxis after ICH significantly reduced the odds of seizure after correcting for pre-admission NIHSS score, age, and sex, but was associated with a longer and more costly hospital stay. Patients were more likely to receive anticonvulsant prophylaxis if patients presented with more severe symptoms or worse lesions on imaging. Prophylaxis did not afford significant improvement in measures of clinical outcome including NIHSS and mRS.

## References

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