Effect of Primary Prophylactic Antiseizure Medication for Seizure Prevention Following Intracerebral Hemorrhage in the ERICH Study

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Abstract

Objectives: Intracerebral hemorrhage (ICH) has the highest morbidity and mortality rate of any stroke subtype and clinicians often administer prophylactic antiseizure medications (ASMs) as a means of preventing post-stroke seizures, particularly following lobar ICH. However, evidence for ASM efficacy in preventing seizures and reducing disability is lacking given limited randomized trials. Herein, we report analysis from a large prospective observational study that evaluates the effect of primary prophylactic ASM administration on seizure occurrence and disability following ICH.

Materials and methods: Primary analysis was performed on 1630 patients with ICH enrolled in the ERICH study. A propensity score for administration of prophylactic ASM was developed and patients were matched by the closest propensity score (difference < 0.1). McNemar's test was used to compare occurrence of in-hospital seizure and disability, defined by modified Rankin Score (mRS) 3 at 3 months post ICH.

Results: Of the 815 matched pairs of patients treated with primary prophylactic ASM, there was no significant difference in seizure occurrence ($p = 0.4631$) or disability ($p = 0.4653$). Subset analysis of 280 matched pairs of patients with primary lobar ICH similarly revealed no significant difference in seizure occurrence ($p = 0.1011$) or disability ($p = 1.00$) between prophylactically treated and untreated patients.

Conclusions: Although current guidelines do not recommend primary prophylactic ASM following ICH, clinical use remains widespread. Data from the ERICH study did not find an association between administering primary prophylactic ASM and preventing seizures or reducing disability following ICH, thus providing evidence to influence clinical practice and patient care.

Introduction

The current utilization of primary prophylactic antiseizure medication (ASM) following intracerebral hemorrhage (ICH) is controversial given the lack of randomized, controlled trials. Although ICH has been shown to have the highest morbidity and mortality rate of any stroke subtype, the prognostic contribution of seizures is largely unknown. Previous reports have identified an independent association, though not causality, between seizures and early ICH expansion,[2] midline shift[3] and functional outcomes.[4] Therefore, clinical practice has often implemented primary prophylactic ASM and widespread use (estimated between 20% and 40%)[5–8] continues despite current guidelines. Our aim in this study was to analyze data from the Ethnic/Racial Variations of Intracerebral Hemorrhage Study (ERICH), one of the largest prospective observational studies of ICH, to evaluate the effect of primary prophylactic ASM administration on seizure occurrence and disability following ICH. The study's large sample size from 19 independent centers afforded us the ability to perform propensity score analysis in a multi-ethnic population with sufficient power for subset analysis in patients with primary lobar hemorrhage. The data presented, herein, provides an evidence-based evaluation of primary prophylactic ASM following ICH and specifically, lobar ICH.

Seizure onset has been shown to occur at various time points after ICH (i.e. weeks, months, or years post-injury). Prevalence of clinically observed seizures has been documented to range from 1.7% to 31% despite primary prophylactic ASM administration[2,3,9] and between 28% and 42% when electrographic seizures were considered.[3,10] Location of ICH, particularly primary lobar hemorrhage which has closer proximity to the cortex, is thought to be correlated with increased risk of seizure occurrence.[1,3,11–18] Meanwhile, size of hemorrhage has been controversially related to seizure occurrence with some reports identifying potential association[19–20] and others not.[14,16] Patients who require neurosurgical interventions after ICH, such as placement of external ventricular drains or surgical evacuation, may have increased risk for seizures.[21,22] Other confounding factors include sepsis, which may itself, in addition to commonly prescribed antibiotics, lower seizure threshold,[23,24] though previous data have not been conclusive. Similarly, heavy

alcohol use or illicit drug use may concurrently lower seizure threshold in patients at time of presentation. The variable prevalence of seizure after ICH and diverse clinical presentations complicate establishing set criteria for initiating a randomized control trial. However, the large multiethnic patient population in the ERICH study allows for propensity score analysis of matched pairs as a means of emulating a randomized trial. In this prospective observational study, we were also able to identify and account for certain confounding factors thought to influence administration of primary prophylactic ASM as well as exclude patients with prior history of epilepsy or ASM use.

Though the use of primary prophylactic ASM has not been recommended by the AHA (Class III; Level B) since 2010, widespread use continues and remains controversial. There appears to be an increased preference for levetiracetam given that prior studies have reported an association between phenytoin administration and worse cognitive outcomes when compared with levetiracetam in patients with ICH.[8,23,25,26] However, clinical practice regarding implementation of ASM prophylaxis should be determined by evidence-based evaluation of treatment efficacy in preventing seizures and ultimately reducing disability. The analyses presented in this paper address the question of whether primary prophylactic ASM can decrease seizure occurrence after ICH and improve long-term outcome, as measured by the modified Rankin Scale (mRS), using the largest dataset available to date.

Methods

The Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) study was a multicenter, prospective, case-control study of self-reported non-Hispanic white, non-Hispanic black and Hispanic patients with ICH that has been previously well described.[27] The study utilized 19 clinical recruitment centers with prior approval by the Institutional Review Board to enroll 3000 patients with ICH from September 2010 to October 2015. A total of 42 sites were involved and recruitment was facilitated by "hot-pursuit": a strategy which involves early identification of cases through active screening of admission logs from the emergency department, general admission logs, neurological intensive care unit, neurology and neurosurgery services to minimize the effect of early mortality following ICH and survival bias. Study participants were 18 years of age residing within 75 miles of one of the recruitment centers. Participants or legal representatives were provided with informed consent in English or Spanish prior to enrollment and subjects were matched 1:1 with control cases by age (+/− 5 years), sex, ethnicity/race, and metropolitan area.

ICH was defined in the study as a spontaneous focal blood collection within the brain parenchyma causing abrupt onset of a severe headache, focal neurologic deficit, or altered level of consciousness.[27,28] Exclusion criteria for enrollment included ICH attributable to trauma, hemorrhagic conversion of ischemic stroke, aneurysm-related, dural venous sinus thrombosis, vascular malformation, malignancy-related coagulopathy, or tumor with hemorrhage. Among items on baseline interview, participants (both cases and controls) were asked to provide information regarding prior diagnosis of epilepsy as well as a list of all medications including use of prior ASMs. Patients who self-reported (or by proxy) prior history of seizure or patients who were first administered ASM for a documented seizure were excluded from the analysis. ASMs were initiated at the discretion of clinicians at

each study site. Data for the analyses presented in this manuscript were obtained from chart abstraction into form sections that distinguished ASM administration for seizure prophylaxis or for a documented seizure. Seizure prevalence during the hospitalization was recorded based on the standard practice of the treatment teams and included either clinically witnessed seizures and/or those captured by electroencephalogram (EEG). Seizure prevalence at 90 days was assessed by questionnaire.

Participant characteristics

Researchers across the centers or their proxies were required to interview enrolled participants using a standardized form as well as chart abstraction. Participants were contacted at 90 days for evaluation of mRS which was used to define disability with modified Rankin Score (mRS) 3. They were also asked about seizure occurrence at 90 days and other complications. From the data collected, characteristics of interest for the present analysis included age, sex, race/ethnicity, location and volume of hemorrhage, presence of intraventricular hemorrhage (IVH), ventriculostomy or surgery during hospitalization, history of ischemic stroke, diabetes, or dementia, sepsis and Glasgow Coma Scale (GCS) on admission, heavy alcohol use or illicit drug use. The following surgical interventions were grouped together for analysis: craniotomy for clot evacuation, stereotactic clot aspiration, and certain other procedures. Heavy alcohol use was defined on the standardized form as self-reported (or by proxy) more than two alcoholic beverages on average per day, drinking 5 drinks in a single setting within the last 90 days or prior history of alcohol abuse. Self-reported (or by proxy) use of illicit drugs or a positive urine toxicology screen on admission was used to define illicit drug use.

Imaging

Neuroimaging obtained from study participants were de-identified at study sites prior to storage on Digital Imaging and Communications in Medicine (DICOM) software and electronic upload to a dedicated workstation at the neuroimaging repository (Massachusetts General Hospital and University of Arizona - Tucson). Centralized analysis was performed by reviewers who were blinded to all clinical information and using Alice software (Parexel Corporation, Waltham, MA). Hemorrhage volume, hemorrhage location (deep (i.e. basal ganglia or thalamus), lobar, brainstem, cerebellum or primary IVH), as well as presence of IVH was measured by planimetric analysis of initial diagnostic CT images as previously published.[29–31]

Outcomes

The primary outcome in this study was defined as documented seizure occurrence, while hospitalized after ICH, in study groups treated with primary prophylactic ASM (Prophylactic ASM) or without primary prophylactic ASM (No Prophylactic ASM). Secondary outcome was defined as disability (loss of functional independence), defined as mRS 3 at 90 days after ICH onset.

Statistical analysis

A propensity score for administration of prophylactic ASM was based on covariates selected a priori based on variables which were thought to influence the clinical decision of providing primary prophylactic ASM (e.g. age, sex, race/ethnicity, ICH volume, location of ICH, presence of IVH, ventriculostomy, surgery, GCS, history of ischemic stroke, diabetes, dementia, sepsis, alcohol use and illicit drug use). A stepwise modeling approach was used to match those individuals, without prior documented or witnessed seizure(s), who received prophylactic ASM with those who did not receive prophylactic ASM. Patients were matched by the closest propensity score with no more than a difference of 0.1. To check that the matches were appropriate, descriptive statistics are presented as mean ± SD, median (IQR) for continuous variables and percentages for categorical variables. Patient characteristics are compared between Prophylactic ASM and No Prophylactic ASM groups with t-test (age) and Wilcoxon rank-sum test (e.g. volume of ICH, GCS). Categorical variables (e.g. sex, race/ethnicity, presence of IVH, ventriculostomy, surgery, history of ischemic stroke, heavy alcohol use, diabetes, dementia, sepsis, and illicit drug use) are compared with Chi-squared test between the groups. Primary analysis was performed on 1630 patients with ICH enrolled in the ERICH study with subset analysis completed in patients with primary lobar hemorrhage ($n = 560$). McNemar's test was used to compare the occurrence of in-hospital seizure and disability, defined by mRS 3 at 90 days post ICH, in the Prophylactic ASM group and No Prophylactic ASM group (P value < 0.05). A similar process was used to calculate the propensity for receiving primary prophylactic ASM and matching among patients with primary lobar hemorrhages, resulting in 280 pairs. McNemar's test was again used to compare the occurrence of in-hospital seizure and disability, defined by mRS 3 at 90 days post ICH, in the Prophylactic ASM group and No Prophylactic ASM group (P value < 0.05). Given that mRS data was not available for all study participants at 3-month follow-up, dichotomized analysis of disability (mRS 3) was only completed for matched pairs with available data ($n = 1208$ patients with ICH; $n = 436$ patients with primary lobar hemorrhage). Additional analyses of disability outcome were performed on all patients with available mRS scores using the Cochran Armitage trend test and an ordinal logistical regression analysis with increasing mRS as an outcome measure.

Results

Three thousand participants enrolled in the ERICH study from September 2010 to October 2015. A total of 2540 patients were available for present analysis after excluding patients with prior history of seizure, documented seizure on admission and those patients who were previously taking ASM as secondary prophylaxis or for any underlying condition(s). Of the final ERICH cohort, 815 case-control pairs were matched based on primary prophylactic treatment with ASM (Prophylactic ASM) or no primary prophylactic ASM (No Prophylactic ASM). Among the study participants, 537 were non-Hispanic black, 555 were Hispanic, and 538 were non-Hispanic white.

We first evaluated the covariates thought to influence the propensity to receive primary prophylactic ASM (Table 1). There were no significant differences, after matching, in the following study characteristics among subjects who received ASM prophylaxis ($n = 815$)

versus those who did not (n = 815): age, volume of ICH, race, sex, lobar location of ICH, presence of IVH, ventriculostomy or surgical intervention, history of ischemic stroke, heavy alcohol use, diabetes, dementia, sepsis at time of intake, illicit drug use or GCS on admission. Using a similar approach to calculate the propensity score, we were able to match those who received primary prophylactic ASM to those who did not in order to emulate a randomized trial among patients who had a primary lobar hemorrhage (Table 2). Table 2 demonstrates excellent matching on those variables for the propensity for using primary prophylactic ASM in patients with primary lobar hemorrhage (n = 560), as there was no significant difference between the matched groups.

Among the 815 patients in the Prophylactic ASM group, 85.3% received levetiracetam (n = 695) and 8.5% received phenytoin (n = 69). Patients who received both levetiracetam and phenytoin accounted for 3.7% patients (n = 30). Meanwhile, 2.6% patients in the Prophylactic ASM group (n = 21) received alternative ASM.

In the matched pair analysis (Fig. 1A), there was no significant difference in seizure prevalence when comparing hospitalized patients who were receiving primary prophylactic ASM versus those who did not receive primary prophylactic ASM (p = 0.4631). Of the 1630 patients in total cohort, 97 individuals (6.0%) had documented seizure(s). Among those patients treated with primary prophylactic ASM, 52 patients (6.4%) had seizures. Meanwhile, 45 patients (5.5%) had seizures in the group of patients not treated with primary prophylactic ASM. Subsequent subset analysis of patients with primary lobar hemorrhage (n = 560) was performed in matched pairs (Fig. 1B). Seizure(s) were reported in 51 individuals with primary lobar hemorrhage (9.1%). Among the matched pairs, seizures were documented in 20 patients (7.1%) in the Prophylactic ASM group and 31 patients in the No Prophylactic ASM group (11.1%). There was no significant difference (p = 0.1011) between the matched pairs when evaluating seizure activity in patients with primary lobar hemorrhage treated with primary prophylactic ASM and those without primary prophylactic ASM.

Unfavorable outcome was defined by the loss of functional independence mRS ≥ 3 at 90 days post ICH. Of the 1208 patients with ICH (Fig. 2A), 401 patients (33.2%) were functionally independent (mRS < 3), and 807 patients (66.8%) were no longer functionally independent (mRS ≥ 3) at 90 days post ICH. Analysis was performed on matched pairs of patients in the Prophylactic ASM and No Prophylactic ASM groups; there was no significant difference between the matched pairs with regards to disability at 90 days post ICH (p = 0.4653). Similar analysis was performed on subset population of patients with primary lobar hemorrhage (Fig. 2B). Among 436 patients with lobar ICH, 172 patients (39.4%) were functionally independent (mRS < 3), and 264 patients (60.6%) were no longer functionally independent (mRS ≥ 3) at 90 days post ICH. No significant difference was found with occurrence of disability at 90 days between the matched pairs in patients with primary lobar hemorrhage (p = 1.000). Analysis of mRS scores using the Cochran Armitage trend test revealed no significant difference between Prophylactic ASM and No Prophylactic ASM groups for the total cohort (p = 0.8551) and primary lobar hemorrhage subset (p = 0.6698). Furthermore, ordinal logistic regression models revealed no significant difference favoring Prophylactic ASM over No Prophylactic ASM in the total cohort (odds ratio 0.99;

95% confidence interval: 0.82–1.18) or primary lobar hemorrhage subset (odds ratio 0.93; 95% confidence interval: 0.68–1.28).

Discussion

As the largest and most ethnically diverse prospective observational study of patients with ICH to date, the present study evaluated the effect of primary prophylactic ASM administration on in-hospital seizure occurrence and 90-day disability by comparing matched pairs (Prophylactic ASM versus No Prophylactic ASM) using propensity scores calculated from multivariable logistic regression. Although primary prophylactic ASM use is often implemented in clinical practice to prevent seizures in patients with ICH, our data reveal no significant difference in seizure occurrence between Prophylactic ASM and No Prophylactic ASM groups (Fig. 1A). Additionally, our data indicate no significant influence of primary prophylactic ASM on 90-day disability after ICH (Fig. 2A). Though the analyses presented herein are consistent with prior studies, the large multi-ethnic patient population in the ERICH study further allowed for exclusion of patients with prior history of epilepsy or ASM use and propensity score analysis was utilized to account for certain confounding factors thought to influence administration of primary prophylactic ASM (Table 1). Furthermore, the analysis of matched pairs allowed us to emulate a randomized trial among patients who had primary lobar hemorrhage (Table 2) which revealed no significant difference for in-hospital seizure occurrence (Fig. 1B) or 90-day disability (Fig. 2B) in patients treated with primary prophylactic ASM.

There are several potential limitations to the analysis presented in this study. First, despite using prospectively collected data, our current study is limited by the retrospective nature of data analysis. Data were obtained from chart abstraction and only available if reported into the ERICH study data collection form for individually enrolled patients by each respective site. Second, there is a possibility of survival bias given the high mortality in ICH patients and the uncertainty of developing post-injury seizures in this population. Of the 1630 patients incorporated into our study analyses, there was no appreciable difference between treatment groups in the "do not resuscitate" code status (Prophylactic ASM: 15.8% yes, 83.2% no, 1.0% unknown; No Prophylactic ASM: 16.0% yes, 82.1% no, 2.0% unknown) nor comfort care designation (Prophylactic ASM: 11.7% yes, 87.1% no, 1.2% unknown; No Prophylactic ASM: 11.5% yes, 86.4% no, 2.1% unknown). The methodology implemented in the ERICH study attempts to reduce survival bias using "hot pursuit" which required patients to be screened and enrolled within 48 hours of admission. While the study's exclusion criteria (e.g., ICH attributable to trauma, hemorrhagic conversion of ischemic stroke, aneurysm-related, dural venous sinus thrombosis, vascular malformation, malignancy-related coagulopathy, or tumor with hemorrhage) was established to avoid confounding variables, it is plausible that patients at risk for seizure development or increased disability were excluded from our data analyses. Furthermore, patients who were lost to follow-up limited the sample size of patients evaluated for 90-day disability between Prophylactic ASM and No Prophylactic ASM groups.

Our present study was not designed to stratify seizure occurrence into categories such as early, late, convulsive or non-convulsive status epilepticus. Previous studies have

reported 4.0% to 23.5% early seizures[10–12,14,23,32–39] compared with 2.6% to 15.6% late seizures[10,14,17,18,20,23,32,38–42] in ICH patients. Prevalence of convulsive status epilepticus in ICH patients has been estimated between 4% and 60%.[1,15,23,37] However, approximately 22% to 76% of ICH patients are thought to have non-convulsive seizures which would be difficult to identify without EEG monitoring.[2,3] Seizure occurrence was identified and documented at the discretion of providers at each study site. Therefore, a documented seizure may have been a witnessed clinical seizure, clinical seizure captured on EEG, or a subclinical seizure captured on EEG. The inconsistent use of electroen-cephalogram (EEG) across the ERICH study may not have captured a proportion of patients having subclinical seizures of uncertain significance. As a result, it is possible that the prevalence of seizures may be underestimated in our sample for this study. Furthermore, the variable prevalence and categorization of seizure subtypes may have implications for determining the utility of primary prophylactic ASM after ICH for a specific subset of patients and their prognosis.

Substantial clinical curiosity has warranted development of scoring systems to help with prognostication. For example, the CAVE Score has been validated to estimate the risk of late seizures > 7 days after ICH based on cortical involvement (1 point), age < 65yrs (1 point), volume > 10cc (1 point) and early seizure < 7 days of ICH (1 point).[43,44] The data analysis presented herein did allow for subset analysis in a large group of patients with primary lobar hemorrhage and revealed no significant difference in seizure occurrence while hospitalized, despite administration of primary prophylactic ASM. While the etiology of ICH was not always reported or determined at the time of chart abstraction, future studies accounting for the etiology of ICH as a determinant of seizure prophylaxis initiation or efficacy may yield useful information. Our data set unfortunately does not allow us to distinguish whether patients had seizure onset early or late in their clinical course, nor the duration of ASM administration in this context of seizure timing as it relates to injury. Subset analysis of ERICH study participants by Kwon et al. found that the risk of developing late seizures following ICH is increased by younger age, large volume hematoma, surgical evacuation and lobar ICH.[44] Future studies may wish to clarify the timing of seizure occurrence to further investigate the utility of the CAVE score in helping predict a subset of patients who may benefit from primary prophylactic ASM after ICH.

Although it has previously been considered that certain factors may increase seizure risk following ICH (i.e. ICH volume and location, surgical intervention, sepsis, heavy alcohol or illicit drug use, etc.), our analysis of data from the ERICH study did not identify a subpopulation of ICH patients which would benefit from primary prophylactic ASM administration. The current study did account for craniotomy for clot evacuation, stereotactic clot aspiration, and certain other procedures. Though surgical interventions have previously been thought to be a risk factor for seizures, likely given the presumption of cortical white matter disruption, our data does not indicate a significant influence of surgical intervention on in-hospital seizure occurrence between the groups. However, our analysis did group various surgical interventions into either surgery or ventriculostomy subsets. Perhaps future studies with larger sample sizes may be able to stratify data based on the specific surgical intervention implemented.

Post hoc analysis of the ERICH study revealed no independent association of primary prophylactic ASM with unfavorable mRS at 90 days,[23] and our data presented herein similarly suggests the same. As a prospective observational study, we were unable to control for ASM selection, dosing range, time of medication initiation (e.g., within 24 hours of admission) or scheduled duration of treatment throughout hospitalization or at the 90-day timepoint. Data entry in this study additionally did not require study sites to report continuous sedative infusions (e.g. propofol, midazolam or pentobarbital) which may have been implemented as antiseizure treatment or for sedative purposes. The use of prophylactic ASM based on admission protocols certainly has the potential to add bias to the study; however, there was only one site of the 19 enrollment centers that administered prophylactic ASM to all lobar hemorrhage patients ($n = 20$) enrolled in the ERICH study. Otherwise, the administration of prophylactic ASM was variable among the centers (Supplemental Table 1).

Most patients enrolled in this study were administered levetiracetam ($n = 695$; 85.3%), though other ASM in descending order of use includes phenytoin, lorazepam, phosphenytoin, and midazolam. There have been reports of phenytoin being associated with worse cognitive and functional outcomes when compared with levetiracetam in patients with ICH.[8,23,25,26] Additional favorable features that have likely contributed to the increased popularity of levetiracetam include more predictable pharmacokinetics and therapeutic range, less reported drug interactions or allergies, and predominantly renal clearance. However, Naidech et al. more recently reported that the administration of prophylactic levetiracetam during hospitalization for ICH was independently associated with lower cognitive function at follow-up when assessed by Neuro-QOL™ (Quality of Life in Neurologic Disorders) as a determinant of health-related quality of life (HRQoL).[45] Although domain-specific HRQoL assessment tools, such as the validated[46] Neuro-QOL™ or PROMIS® (NIH Patient-Reported Outcomes Measurement Information System), provide meaningful information that may not be captured by ordinal versus dichotomous forms of the mRS, widespread utilization into clinical trials may be limited due to the self-reported subjectivity and cumbersome administration. Future prospective trials may benefit from incorporating diverse patient-centered outcome measurement tools and may also consider either dose-response or dose-escalation study designs to further evaluate the effect of ASM on seizure occurrence and disability following ICH.

Summary (Conclusions)

The variable onset and prevalence of seizure after ICH undeniably complicates establishing set criteria for treatment guidelines. In 1999, the AHA guidelines proposed 1-month administration of primary prophylactic ASM followed by a taper or discontinuation if there was no clinical evidence of seizure activity during that time (Level of Evidence V, Grade C Recommendation).[47] Almost 10 years later, in 2007, the AHA recommendation for primary prophylactic ASM after ICH was primarily thought to reduce the risk of early seizures and specifically in those patients with lobar ICH.[48] Updated guidelines in 2010 suggested that data to support primary prophylactic ASM administration after ICH was limited in terms of long-term benefit of neurologic outcome, prevention of seizures and mortality.[9,25,49] Thus, the AHA's only Class I recommendations for ASM implementation is in patients with

seizures (Class I; Level A) and patients with a change in mental status with electrographic evidence of seizures on EEG (Class I; Level C).[49]

Gilmore et al proposed an algorithmic approach to implementing seizure prophylaxis with risk stratification based on clinical, radiographic and encephalographic parameters and repeated assessments to guide therapy initiation or duration.[23] This algorithm aligns with the AHA recommendation and is further supported by the analyses presented in this paper. Our clinical practice regarding implementation of ASM should be based on evidence-based data regarding treatment efficacy in preventing seizures and ultimately reducing disability. Data from the large prospective ERICH study did not find an association between administering primary prophylactic ASM and preventing seizure prevalence or reducing disability following ICH and even more specifically, primary lobar hemorrhage. Thus, the analysis presented from the largest and most ethnically diverse prospective observational study of patients with ICH to date provides additional evidence to influence clinical practice and patient care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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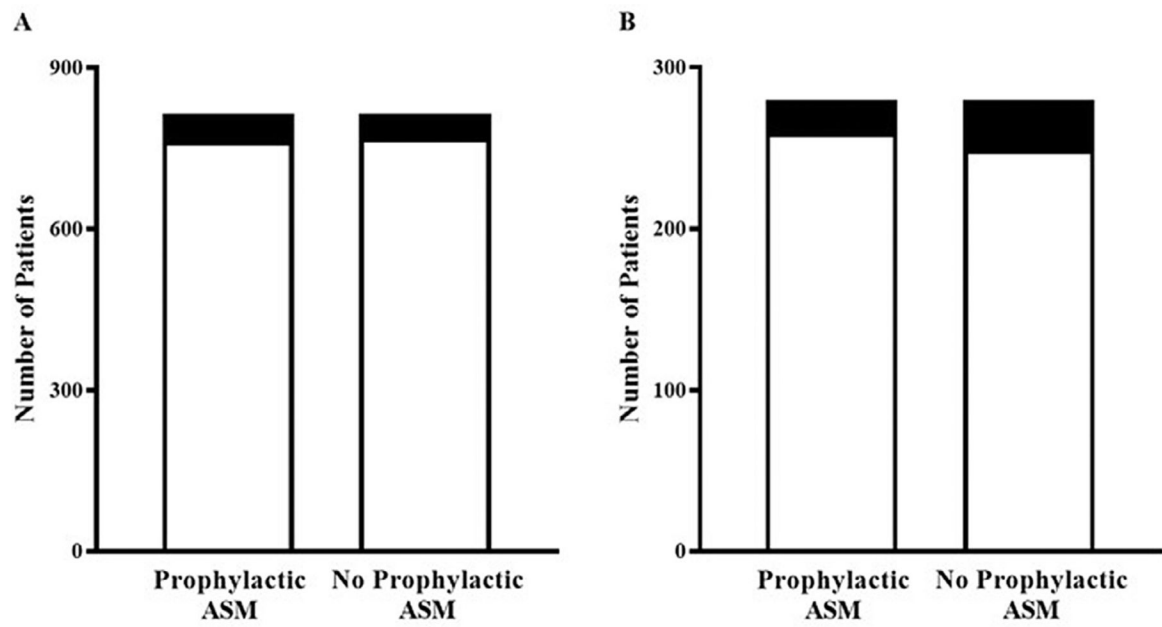
Fig. 1.

Primary prophylactic ASM did not reduce seizure occurrence among (A) total ICH patients (n = 1630) or in a subset analysis of (B) primary lobar hemorrhage patients (n = 560) during their initial hospitalization.
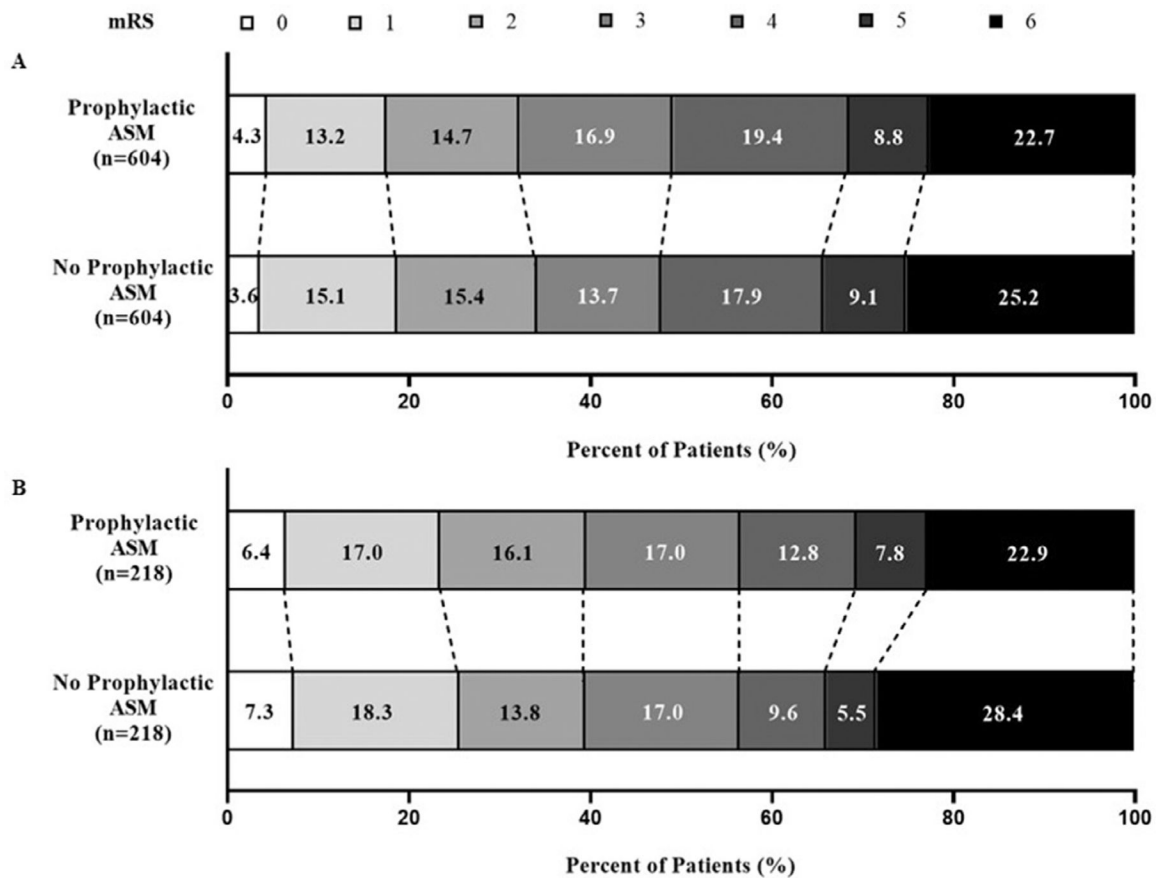
Legend: ☐ No Seizure ■ Seizure

Fig. 2.
Primary prophylactic ASM administration did not significantly influence disability (mRS ≥ 3) at 90 days among total ICH patients (A; n = 1208) or patients with primary lobar hemorrhage (B; n = 436).

Table 1.

Demographic data and clinical characteristics of total cohort (ñ = 1630) after propensity score modeling in Prophylactic ASM and No Prophylactic ASM groups. Data represents n (%) unless otherwise noted. Abbreviations: SD – standard deviation, cc – cubic centimeter volume, IQR – interquartile range, IVH – intraventricular hemorrhage, GCS – Glasgow coma scale.

Variable	Prophylactic ASM (n = 815)	No Prophylactic ASM (n = 815)	P-value
Age: Mean ± SD	62.0 ± 14.9	61.4 ± 14.8	0.43
Sex			0.29
Female	348 (42.7)	327 (40.1)	
Male	467 (57.3)	488 (59.9)	
Race/Ethnicity			0.97
White non-Hispanic	270 (33.1)	268 (32.9)	
Black non-Hispanic	270 (33.1)	267 (32.8)	
Hispanic	275 (33.7)	280 (34.4)	
Volume (cc): Median; IQR	15.1; 6.0–32.5	13.9; 6.5–30.3	0.64
Lobar Location	307 (37.7)	296 (36.3)	0.57
Presence of IVH	380 (46.6)	393 (48.2)	0.52
Ventriculostomy	191 (23.4)	196 (24.0)	0.77
Surgery	74 (9.1)	73 (9.0)	0.93
History of Ischemic Stroke	82 (10.1)	98 (12.0)	0.21
Heavy Alcohol Use	88 (11.0)	73 (9.2)	0.23
Diabetes	231 (28.4)	208 (25.6)	0.20
Dementia	33 (4.0)	35 (4.3)	0.80
Sepsis	41 (5.0)	35 (4.3)	0.48
Illicit Drug Use	95 (11.7)	89 (10.9)	0.64
GCS: Median; IQR	14; 10—15	14; 10—15	0.70

Table 2.

Demographic data and clinical characteristics of matched pairs after propensity score modeling of patients with primary lobar hemorrhage (n = 560) in Prophylactic ASM and No Prophylactic ASM groups. Data represents n (%) unless otherwise noted. Abbreviations: SD – standard deviation, cc – cubic centimeter volume, IQR – interquartile range, IVH – intraventricular hemorrhage, GCS – Glasgow coma scale.

Variable	Prophylactic ASM (*n* = 280)	No Prophylactic ASM (*n* = 280)	*P*-value
Age: Mean ± SD	66.3 ± 15.0	68.0 ± 14.9	0.17
Sex			1.00
Female	141 (50.4)	141 (50.4)	
Male	139 (49.6)	139 (49.6)	
Race/Ethnicity			0.06
White non-Hispanic	123 (43.9)	146 (52.1)	
Black non-Hispanic	77 (27.5)	55 (19.6)	
Hispanic	80 (28.6)	79 (28.2)	
Volume (cc): Median; IQR	24.2; 11.2–49.6	22.9; 10.9–50.8	0.71
Presence of IVH	92 (32.9)	80 (28.6)	0.27
Ventriculostomy	16 (5.7)	15 (5.4)	0.85
Surgery	31 (11.1)	23 (8.2)	0.25
History of Ischemic Stroke	32 (11.4)	37 (13.2)	0.52
Heavy Alcohol Use	18 (6.5)	13 (4.7)	0.35
Diabetes	71 (25.4)	80 (28.6)	0.39
Dementia	22 (7.9)	27 (9.6)	0.45
Sepsis	4 (1.4)	9 (3.2)	0.16
Illicit Drug Use	18 (6.4)	18 (6.4)	1.00
GCS: Median; IQR	14; 12—15	15; 12—15	0.61