HHS Public Access

Author manuscript

Neurocrit Care. Author manuscript; available in PMC 2019 May 16.

Published in final edited form as:

Neurocrit Care. 2017 October ; 27(2): 220–228. doi:10.1007/s12028-017-0385-8.

Prophylactic Anticonvulsants in Intracerebral Hemorrhage

Jason Mackey, MD MS[1,2], **Ashley D. Blatsioris, MPA**[1], **Elizabeth A.S. Moser, MS**[3], **Ravan J.L. Carter, BS**[2], **Chandan Saha, PhD**[3], **Alec Stevenson, BS**[1], **Abigail L. Hulin, BSN**[1], **Darren P. O'Neill, MD**[4], **Aaron A. Cohen-Gadol, MD**[5], **Thomas J. Leipzig, MD**[5], and **Linda S. Williams, MD**[1,2,6]

[1]Department of Neurology, Indiana University School of Medicine, Indianapolis, IN

[2]Regenstrief Institute, Indianapolis, IN

[3]Department of Biostatistics, Indiana University School of Medicine, Indianapolis, IN

[4]Department of Radiology, Indiana University School of Medicine, Indianapolis, IN

[5]Department of Neurosurgery, Indiana University School of Medicine, Indianapolis, IN

[6]Richard L. Roudebush VA Medical Center

Abstract

Background and Purpose: Prophylactic anticonvulsants are routinely prescribed in the acute setting for ICH patients, but some studies have reported an association with worse outcomes. We sought to characterize the prevalence and predictors of prophylactic anticonvulsant administration after ICH as well as guideline adherence. We also sought to determine if prophylactic anticonvulsants were independently associated with poor outcome.

Methods: We performed a retrospective study of primary ICH in our two academic centers. We used a propensity matching approach to make treated and non-treated groups comparable. We conducted multiple logistic regression analysis to identify independent predictors of prophylactic anticonvulsant initiation and its association with poor outcome as measured by modified Rankin score.

Results: We identified 610 patients with primary ICH, of whom 98 were started on prophylactic anticonvulsants. Levetiracetam (97%) was most commonly prescribed. Age (OR: 0.97, 95% CI: 0.95–0.99, p < .001), lobar location (OR: 2.94, 95% CI: 1.76–4.91, p < .001), higher initial NIHSS score (OR: 2.31, 95% CI: 1.40–3.79, p = .001), craniotomy (OR: 3.06, 95% CI: 1.51–6.20, p = .002) and prior ICH (OR: 2.36, 95% CI: 1.10–5.07, p = .028) were independently associated with prophylactic anticonvulsant initiation. Prophylactic anticonvulsant use was not associated with worse functional outcome (mRS 4–6) at hospital discharge or with increased case-fatality. There was no difference in prescribing patterns after 2010 guideline publication.

Corresponding author: Jason Mackey, MD MS, 355 West 16th St, Suite 3200, Indianapolis, IN 46202, 317-962-5913 (phone), 317-962-2141 (fax), jsmackey@iupui.edu.

Conflict of Interest/Disclosures

Dr. O'Neill reports no disclosures.

Dr. Cohen-Gadol reports no disclosures.

Dr. Leipzig reports no disclosures.

Dr. Williams reports no disclosures.

Discussion: Levetiracetam was routinely prescribed following ICH and was not associated with worse outcomes. Future investigations should examine the effect of prophylactic levetiracetam on cost and neuropsychological outcomes as well as the role of continuous EEG in identifying subclinical seizures.

Keywords

intracerebral hemorrhage; outcomes; anticonvulsants; health services; guideline adherence

Introduction:

Intracerebral hemorrhage (ICH) has high morbidity and mortality[1] and treatment remains largely supportive. Seizures are a common complication in the acute setting[2] and prophylactic treatment with anticonvulsants is common,[3] though the guidelines have recommended that patients without seizures should not receive prophylactic anticonvulsants.[4, 5] Whether prophylactic anticonvulsants are associated with poor outcome in ICH remains unclear.[3, 6–9] We therefore sought to identify factors associated with prophylactic anticonvulsant initiation and to determine whether prophylactic anticonvulsants were independently associated with poor clinical outcome. We also sought to evaluate whether prophylactic anticonvulsant prescribing patterns changed after guideline publication in 2010.

Methods:

This study was approved by the Indiana University Institutional Review Board, the Indiana Network for Patient Care (INPC) board of directors, and Wishard Memorial Hospital.

Cohort assembly

We evaluated all patients ≥18 years old with primary ICH presenting to two academic centers via a query of the INPC database (http://www.ihie.org). The INPC is a health information exchange serving multiple hospital systems in Central Indiana.[10] For inclusion in the study the index ICH had to occur between January 1, 2009 and December 31, 2011; we additionally queried the database until February 29, 2012 to identify patients with an index ICH during the study period but who were subsequently discharged in the following two months. We used discharge ICD-9 codes of 431 and 432.9 to identify potential cases; these codes have >85% sensitivity for the identification of patients with ICH.[11] A vascular neurologist (J.M.) reviewed the medical record and imaging scans of all potential cases to ensure proper case characterization. Patients with evidence of traumatic ICH or an aneurysm, encephalitis, or brain tumor as a cause of the hemorrhage were excluded. Patients with hemorrhagic transformation of an ischemic infarct or hemorrhage due to venous sinus thrombosis, carotid endarterectomy, or thrombolytic administration for ischemic stroke were also excluded.

Clinical data abstraction

Under the close supervision of a vascular neurologist, data abstractors ascertained via standardized chart review demographic data, vascular risk factors, and processes of care. All available referring hospital and transfer data were reviewed. If a formal NIH stroke scale

(NIHSS) score was not reported at presentation we used a validated method for estimation.[12] The neurologist reviewed the initial imaging scan from the academic center for each patient as well as all available imaging scans from the referring hospital. Hematoma volume was calculated with the ABC/2 method.[13]

Clinical outcome measures included modified Rankin score (mRS) at discharge. Date, time, and cause of death were recorded for patients who died during the hospitalization. Discharge disposition was also recorded. We determined vital status via present-day chart review and obituary query. We then performed a National Death Index (http://www.cdc.gov/nchs/ndi.htm) query for the vital status of all patients for whom we still could not account. All clinical data were recorded in REDCap.[14]

Prophylactic anticonvulsant abstraction

For the prophylactic anticonvulsant analysis, we excluded patients with a history of seizure, those with witnessed or suspected seizures, and those with baseline mRS of 4 or 5. We identified time and location for first prophylactic anticonvulsant use and abstracted all medications and doses for the duration of the hospitalization. For each day we calculated the daily dose of the prophylactic anticonvulsants using the World Health Organization defined daily dose (DDD) classification for levetiracetam (1500mg), phenytoin (300mg), and fosphenytoin (450mg), (http://www.whocc.no/ddd/definition_and_general_considera/), as well as the number of dose days, the average daily dose, and the cumulative dose for each patient. For example, if a patient received levetiracetam 500mg BID for a total of 3 days the mean daily dose would be 0.67 (1000/1500) and the cumulative dose would be 2 (0.67*3). We also reviewed all available documentation to determine whether the patient was discharged on the prophylactic anticonvulsant. We further reviewed the entirety of the available medical record and abstracted the last known prophylactic anticonvulsant administration.

Statistical Methods

Our two dichotomous primary outcomes were whether a patient had a prophylactic anticonvulsant administered and whether a patient had worse functional outcome at hospital discharge as measured by mRS of 4–6. We assembled the prophylactic anticonvulsant cohort for the first primary outcome and the functional outcome cohort for the second primary outcome as described below. To analyze the functional outcome data, we assessed how comparable the treatment and corresponding matched control groups were at baseline. Chi-square, Fisher's exact, Student's t, or Wilcoxon rank sum tests were used for this comparison. We considered several covariates as listed in Table 1 to identify factors associated with each of the two primary outcomes and used univariate and multiple logistic regression analyses. These variables included general patient characteristics, variables significant in previous studies, and variables which treating physicians may have considered as predisposing patients to higher seizure risk. We assessed the association at univariate level and the covariates found to be significant at a p-value of <0.20 were included in a stepwise multiple logistic regression model. Statistical analyses were performed with SAS version 9.4 (SAS institute, Cary NC).

Prophylactic anticonvulsant analysis cohort assembly (total n=506)

Of the 610 patients in the overall cohort, 41 (6.7%) were excluded because of a previous history of seizures and 45 (7.4%) had a witnessed or suspected seizure associated with the index ICH prior to anticonvulsant initiation. An additional 18 patients were excluded from this analysis because the baseline mRS was 4 (n=16) or 5 (n=2). The final cohort therefore included 506 patients, with 98 who were administered a prophylactic anticonvulsant and 408 who were not administered a prophylactic anticonvulsant.

Functional outcome analyses cohort assembly (total n=186)

We then constructed a control group of patients (a group of patients not treated with prophylactic anticonvulsants) who would be as comparable to the treated group of patients as possible. We used the propensity score based matching approach and matched each treated patient to a control patient if the difference in propensity score was within a pre-defined standard propensity score caliper. Using calipers of width equal to 0.2 of the pooled standard deviation of the logit of the propensity score removes about 99% of the bias due to the measured confounders.[15] For each treated patient we selected a control patient if the absolute difference of the propensity score on the logit scale was within 0.2 of the pooled standard deviation of the logit of the propensity score. The matching was done without replacement. We identified 93 control patients as a match to 93 treated patients. We could not identify a suitable match for 5 of the treated patients.

Results:

We identified 506 patients with primary ICH from 2009 to 2011, of whom 98 (19.4%) were given a prophylactic anticonvulsant, and 408 (80.6%) who were not given a prophylactic anticonvulsant. Of the 98 given a prophylactic anticonvulsant, 45 (45.9%) presented to a referring hospital initially. The mean age was 61.5, 50 (51.0%) were women, and 33 (33.7%) were black. Mean ICH volume was 28.5mL and 52 (53.1%) had intraventricular extension. Overall 22 (22.5%) patients died in the hospital and 40 (40.8%) died in the first year following ICH.

Of the 408 not given a prophylactic anticonvulsant, 272 (66.7%) presented to a referring hospital initially. The mean age was 67.2, 184 (45.1%) were women, and 100 (24.5%) were black. Mean ICH volume was 18.8mL and 191 (46.8%) had intraventricular extension. Overall 79 (19.4%) patients died in the hospital and 153 (37.5%) died in the first year following ICH.

Prophylactic anticonvulsant analysis

Levetiracetam alone was prescribed in 95 of 98 (97%) cases; one patient was prescribed both levetiracetam and phenytoin, one was prescribed phenytoin alone, and one was prescribed phenytoin and a single dose of fosphenytoin. Initiation of prophylactic anticonvulsants occurred in the ICU (61, 62.2%), academic center ED (26, 26.5%), on the hospital floor (5, 5.1%), in the operating room (4, 4.1%), and at the outside hospital (2, 2%).

The univariate analysis assessing association of factors with initiation of prophylactic anticonvulsant is shown in Table 1. Younger age, lower baseline mRS, lower GCS, higher NIHSS score, greater ICH volume, supratentorial ICH, lobar location, and craniotomy were associated with prophylactic anticonvulsant use. The multiple logistic regression analysis is shown in Table 2. Younger age, craniotomy, prior ICH, higher NIHSS score, and lobar location were independently associated with prophylactic anticonvulsant initiation.

Duration and intensity subanalysis

For the 98 patients prescribed prophylactic anticonvulsants, the mean and median duration of treatment in the hospital was 11.7 days and 6.5 days, respectively. The mean daily dose and median daily dose were 0.6125 and 0.6132, respectively. The median cumulative dose was 4.0 (1.7, 9.0).

Functional outcomes analyses

After using the propensity score based matching approach, the treated and control groups were found to be very similar in demographic characteristics and clinical outcomes as shown in Table 3. Univariate and multiple logistic regression analyses results for association with worse mRS of 4–6 are shown in Tables 4 and 5, respectively. Prophylactic anticonvulsant initiation was not associated with worse functional outcome of mRS either in unadjusted or adjusted analyses for other significant predictors of mRS. Higher NIHSS score, greater ICH volume, intraventricular extension, and worse baseline mRS were independently associated with worse functional outcome of mRS at discharge.

Prophylactic anticonvulsants were also not associated with higher inpatient case-fatality or with case-fatality at one year in univariate analysis (data not shown).

Prophylactic anticonvulsants at discharge and afterward

Of the 98 patients started on prophylactic anticonvulsants, 2 (2%) had a subsequent seizure during the admission and 74 of the 96 remaining (77.1%) survived to discharge. Of the 42 (56.8%) patients discharged from the hospital on a prophylactic anticonvulsant, 13 (31%) were still on an anticonvulsant at 3 months and 6 (14.3%) were still on an anticonvulsant at 1 year following index ICH.

Guideline implementation

We also dichotomized the study time period into before and after online 2010 guideline publication (online July 22, 2010)[4] to assess the effect of the guideline on anticonvulsant prescribing patterns. Of 284 patients admitted prior to online ICH guideline publication, 55 (19.4%) were given prophylactic anticonvulsants compared with 43 of 222 (19.4%) after.

Discussion:

We found that levetiracetam was routinely prescribed in our ICH population and that there was no association with worse outcomes at hospital discharge or at one year. From a resource utilization standpoint, prophylactic anticonvulsants were very commonly continued through hospital discharge and, in some cases, months or even years afterward. We also

found no significant change in prescribing habits after a new guideline recommended against prophylaxis in 2010.

Several studies in recent years have evaluated the prevalence and predictors of anticonvulsant prophylaxis in ICH as well as a potential association with poor outcome. Prevalence of prophylaxis has generally ranged from 20–40%.[7, 8, 16, 17] In one study investigators evaluated 295 subjects from the placebo arm of the CHANT trial and found that prophylactic anticonvulsants were independently associated with a very poor outcome (mRS of 5 or 6.)[3] The most commonly prescribed anticonvulsant was phenytoin. Another large study, also predominantly with phenytoin, found that prophylactic anticonvulsants were associated with reduced 90-day mortality and improved 90-day functional outcome, but these associations disappeared when the analysis was restricted to patients surviving beyond five days in an effort to diminish confounding by indication.[7]

More recent studies have evaluated levetiracetam in ICH patients. A prospective study of 98 patients, of whom 40 received prophylactic anticonvulsants, found that phenytoin was associated with poor outcome (mRS 4–6) at 3 months but that levetiracetam was not. This study also evaluated duration and intensity of therapy and reported a median duration of about 1 week. Most patients receiving levetiracetam were prescribed 500mg BID.[6] Other studies comparing levetiracetam and phenytoin have found that levetiracetam was associated with improved cognitive outcomes at discharge and fewer seizures[18] as well as improved long-term outcomes.[19] A large study using a portion of the ERICH cohort found that prophylactic levetiracetam was not independently associated with poor outcome. After adjustment for multiple factors associated with poor outcome, prophylactic levetiracetam was not associated with worse functional outcome at 3 months.[8]

Our study confirms these findings and extends them by including a rigorous propensity score matching analysis to our outcome models. Levetiracetam is a newer anticonvulsant whose precise mechanism of action is unclear. Levetiracetam has fewer side effects and drug interactions than phenytoin.[20] A recent multicenter study found that levetiracetam use increased between 2007 and 2012 with a corresponding decrease in phenytoin use,[17] which may reflect changes in prescribing behavior based on a study suggesting potential harm from phenytoin.[6] That we did not identify an association with levetiracetam and adverse outcomes is unsurprising but reassuring nonetheless.

Strengths of this study include a large, well-characterized cohort, extensive review of referring hospital data, and a pre- and post-guideline publication timeframe, as well as the rigorous methodology noted above. There are several limitations to this work. This study is retrospective in nature with the well-known inherent limitations. Prophylactic anticonvulsant initiation was not randomized and was left to the discretion of the treating physician, though we attempted to adjust for that using propensity matching. There may also be other factors, such as individual physician prescribing habits, that play a role in prophylactic anticonvulsant initiation for which we cannot account in this study. Finally, because we did not systematically evaluate patients with continuous EEG misclassification bias is possible.

In this large retrospective study we found that prophylactic levetiracetam was commonly prescribed in our ICH population and that it was not associated with poor functional outcomes at hospital discharge or with one-year case-fatality. Future investigations should examine the effect of levetiracetam on cost and whether continuous EEG monitoring adds to decision-making about anticonvulsants in patients with ICH. Study of the impact of prolonged levetiracetam on quality of life and neuropsychological outcomes in ICH patients is also warranted as longer exposure could be deleterious. Because there are few specific treatments for ICH, more health services research, including guideline adherence research, in ICH is needed as well. Finally, only a randomized controlled trial will be able to answer definitively whether ICH patients benefit from prophylactic anticonvulsants.

Acknowledgments

Sources of Funding

This work was supported by awards from the IU Health Values Fund (IUH VFR365), the IU CTSI PDT (ICTSI NIH/NCRR RR025761), the IUH/IUSM Strategic Research Initiative, and an IU CTSI KL2 award (NIH, UL1TR001108, Shekhar PI).

Dr. Mackey is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative, and CTSI PDT. NIH LRP recipient. Indiana University CTSI KL2 award recipient.

A.D. Blatsioris is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative.

E.A.S. Moser is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative.

R.J.L. Carter is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative.

C. Saha is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative.

A. Stevenson is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative.

A.L. Hulin is funded by Research Grant; Significant; IUH-VFR-365, IUH/IUSM Strategic Research Initiative.

References:

1. van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: A systematic review and meta-analysis. Lancet Neurol 2010;9:167–176 [PubMed: 20056489]
2. Szaflarski JP, Rackley AY, Kleindorfer DO, Khoury J, Woo D, Miller R, et al. Incidence of seizures in the acute phase of stroke: A population-based study. Epilepsia 2008;49:974–981 [PubMed: 18248443]
3. Messé SR, Sansing LH, Cucchiara BL, Herman ST, Lyden PD, Kasner SE, et al. Prophylactic antiepileptic drug use is associated with poor outcome following ich. Neurocrit Care 2009;11:38–44 [PubMed: 19319701]
4. Morgenstern LB, Hemphill JC, Anderson C, Becker K, Broderick JP, Connolly ES, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. Stroke 2010;41:2108–2129 [PubMed: 20651276]
5. Hemphill JC, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2015
6. Naidech AM, Garg RK, Liebling S, Levasseur K, Macken MP, Schuele SU, et al. Anticonvulsant use and outcomes after intracerebral hemorrhage. Stroke 2009;40:3810–3815 [PubMed: 19797183]

7. Battey TW, Falcone GJ, Ayres AM, Schwab K, Viswanathan A, McNamara KA, et al. Confounding by indication in retrospective studies of intracerebral hemorrhage: Antiepileptic treatment and mortality. Neurocrit Care 2012;17:361–366 [PubMed: 22965324]
8. Sheth KN, Martini SR, Moomaw CJ, Koch S, Elkind MS, Sung G, et al. Prophylactic antiepileptic drug use and outcome in the ethnic/racial variations of intracerebral hemorrhage study. Stroke 2015:3532–3535 [PubMed: 26470777]
9. Gilmore EJ, Maciel CB, Hirsch LJ, Sheth KN. Review of the utility of prophylactic anticonvulsant use in critically ill patients with intracerebral hemorrhage. Stroke 2016;47:2666–2672 [PubMed: 27608820]
10. McDonald CJ, Overhage JM, Barnes M, Schadow G, Blevins L, Dexter PR, et al. The indiana network for patient care: A working local health information infrastructure. Health Affairs 2005;24:1214–1220 [PubMed: 16162565]
11. Alwell K, Khoury J, Moomaw C, Kleindorfer D, Woo D, Flaherty M, et al. Icd-9 codes positive predictive value for stroke subtypes in a population-based epidemiology study Stroke 2009;40:e183
12. Williams LS, Yilmaz EY, Lopez-Yunez AM. Retrospective assessment of initial stroke severity with the nih stroke scale. Stroke 2000;31:858–862 [PubMed: 10753988]
13. Kothari RU, Brott T, Broderick JP, Barsan WG, Sauerbeck LR, Zuccarello M, et al. The abcs of measuring intracerebral hemorrhage volumes. Stroke 1996;27:1304–1305 [PubMed: 8711791]
14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (redcap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–381 [PubMed: 18929686]
15. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. The American Statistician 1985;39:33–38
16. Reddig RT, Nixdorf KE, Jensen MB. The prophylactic use of an antiepileptic drug in intracerebral hemorrhage. Clin Neurol Neurosurg 2011;113:895–897 [PubMed: 21824722]
17. Naidech AM, Beaumont J, Jahromi B, Prabhakaran S, Kho A, Holl JL. Evolving use of seizure medications after intracerebral hemorrhage: A multicenter study. Neurology 2017;88:52–56 [PubMed: 27864524]
18. Taylor S, Heinrichs RJ, Janzen JM, Ehtisham A. Levetiracetam is associated with improved cognitive outcome for patients with intracranial hemorrhage. Neurocrit Care 2011;15:80–84 [PubMed: 20890680]
19. Szaflarski JP, Sangha KS, Lindsell CJ, Shutter LA. Prospective, randomized, single-blinded comparative trial of intravenous levetiracetam versus phenytoin for seizure prophylaxis. Neurocrit Care 2010;12:165–172 [PubMed: 19898966]
20. Brophy GM, Human T, Shutter L. Emergency neurological life support: Pharmacotherapy. Neurocrit Care 2015;23 Suppl 2:S48–68 [PubMed: 26438454]

Table 1:

Univariate logistic regression for prophylactic anticonvulsant (PA) administration

	Not Prescribed PA (N = 408) N (%)	Prescribed PA (N = 98) N (%)	Unadjusted OR (95% CI) for predicting PA	p-value
Age	-	-	0.97 (0.96, 0.99)	<.001
Sex				.292
Female	184 (78.6%)	50 (21.4%)	1.27 (0.82, 1.97)	
Male	224 (82.4%)	48 (17.6%)	1.00 (– –)	
Race				.065
Black	100 (75.2%)	33 (24.8%)	1.56 (0.97, 2.52)	
Non-Black	308 (82.6%)	65 (17.4%)	1.00 (– –)	
Baseline mRS				.026
0–1	287 (78.2%)	80 (21.8%)	1.87 (1.08, 3.26)	
2–3	121 (87.1%)	18 (12.9%)	1.00 (– –)	
GCS	-	-	0.93 (0.88, 0.98)	.007
Initial NIHSS				.002
≤ 7 (median)	223 (86.1%)	36 (13.9%)	1.00 (– –)	
> 7	185 (74.9%)	62 (25.1%)	2.08 (1.32, 3.27)	
ICH volume (mL)				<.001
Q1 (0–2.3)	117 (90.0%)	13 (10.0%)	1.00 (– –)	
Q2 (2.4–10.1)	106 (86.2%)	17 (13.8%)	1.44 (0.67, 3.11)	
Q3 (10.2–27.0)	99 (78.6%)	27 (21.4%)	2.45 (1.20, 5.01)	
Q4 (27.1–187.5)	84 (67.2%)	41 (32.8%)	4.39 (2.22, 8.71)	
Subarachnoid extension				.317
Yes	40 (75.5%)	13 (24.5%)	1.41 (0.72, 2.75)	
No	368 (81.2%)	85 (18.8%)	1.00 (– –)	
Intraventricular extension				.267
Yes	191 (78.6%)	52 (21.4%)	1.28 (0.83, 2.00)	
No	217 (82.5%)	46 (17.5%)	1.00 (– –)	
Supratentorial				.012
Yes	340 (78.7%)	92 (21.3%)	3.35 (1.31, 8.58)	
No	62 (92.5%)	5 (7.5%)	1.00 (– –)	
Lobar				<.001
Yes	137 (72.9%)	51 (27.1%)	2.15 (1.37, 3.36)	
No	265 (85.2%)	46 (14.8%)	1.00 (– –)	
Initial SBP, mmHg				.403
Q1 (86–155)	104 (83.9%)	20 (16.1%)	1.00 (– –)	

	Not Prescribed PA (N = 408) N (%)	Prescribed PA (N = 98) N (%)	Unadjusted OR (95% CI) for predicting PA	p-value
Q2 (156–178)	107 (82.9%)	22 (17.1%)	1.07 (0.55, 2.08)	
Q3 (179–210)	93 (76.2%)	29 (23.8%)	1.62 (0.86, 3.06)	
Q4 (211–282)	95 (79.2%)	25 (20.8%)	1.37 (0.71, 2.62)	
Initial DBP, mmHg				.514
Q1 (36–81)	105 (84.7%)	19 (15.3%)	1.00 (– –)	
Q2 (82–98)	105 (78.4%)	29 (21.6%)	1.53 (0.81, 2.89)	
Q3 (99–113)	96 (81.4%)	22 (18.6%)	1.27 (0.65, 2.48)	
Q4 (114–183)	92 (78.0%)	26 (22.0%)	1.56 (0.81, 3.00)	
Charlson				.943
0–1	268 (80.7%)	64 (19.3%)	1.00 (– –)	
>1	140 (80.5%)	34 (19.5%)	1.02 (0.64, 1.62)	
Craniotomy				<.001
Yes	23 (53.5%)	20 (46.5%)	4.28 (2.24, 8.17)	
No	384 (83.1%)	78 (16.9%)	1.00 (– –)	
Prior ICH				.081
Yes	28 (70.0%)	12 (30.0%)	1.89 (0.92, 3.86)	
No	379 (81.5%)	86 (18.5%)	1.00 (– –)	
Prior ischemic stroke				.068
Yes	78 (87.6%)	11 (12.4%)	1.00 (– –)	
No	329 (79.1%)	87 (20.9%)	1.88 (0.96, 3.68)	

Table 2:

Predictors of prophylactic anticonvulsant initiation

Model	OR (95% CI)	p-value
Age	0.97 (0.95, 0.99)	<.001
Craniotomy		.002
Yes	3.06 (1.51, 6.20)	
No	1.00 (– –)	
Initial NIHSS		.001
≤ 7 (median)	1.00 (– –)	
>7	2.31 (1.40, 3.79)	
Lobar		<.001
Yes	2.94 (1.76, 4.91)	
No	1.00 (– –)	
Prior ICH		.028
Yes	2.36 (1.10, 5.07)	
No	1.00 (– –)	

Table 3:

Propensity-matched anticonvulsant prophylaxis vs. no prophylaxis

	Prophylactic anticonvulsants N=93	No prophylaxis N=93	p-value
Age, mean (SD)	62.3 ± 13.5	62.0 ± 14.4	.908
Female	47 (50.5%)	50 (53.8%)	.660
Black	32 (34.4%)	28 (30.1%)	.530
Baseline mRS, median (IQR)	1 (0, 1)	1 (0, 1)	.842
GCS, median (IQR)	13 (9, 15)	14 (9, 15)	.729
Initial NIHSS, median (IQR)	12 (4, 19)	9 (3, 26)	.634
ICH volume (mL), median (IQR)	21.9 (7.5, 39.4)	17.5 (5.0, 44.7)	.778
Subarachnoid extension	13 (14.0%)	15 (16.1%)	.682
Intraventricular extension	50 (53.8%)	54 (58.1%)	.555
Supratentorial	87 (93.5%)	83 (89.2%)	.296
Lobar	46 (49.5%)	45 (48.4%)	.883
Initial SBP, mmHg (SD)	187.7 ± 37.5	185.8 ± 42.8	.748
Initial DBP, mmHg (SD)	104.2 ± 27.0	103.3 ± 28.2	.833
Charlson, median (IQR)	1 (0, 2)	1 (0, 2)	.985
Craniotomy	15 (16.1%)	16 (17.2%)	.844
Prior ICH	11 (11.8%)	15 (16.1%)	.398
Prior ischemic stroke	11 (11.8%)	14 (15.1%)	.519

Table 4:

Univariate logistic regression for poor functional outcomes (mRS 4–6) using propensity-matched cohort (N=186)

	mRS 0–3 (N = 53)	mRS 4–6 (N = 133)	Unadjusted OR (95% CI) for predicting mRS 4–6	p-value
	N (%)	N (%)		
Age				.097
Q1 (22–53)	19 (38.8%)	30 (61.2%)	1.00 (– –)	
Q2 (54–62)	16 (30.8%)	36 (69.2%)	1.43 (0.63, 3.25)	
Q3 (63–71)	11 (28.2%)	28 (71.8%)	1.61 (0.65, 3.98)	
Q4 (72–95)	7 (15.2%)	39 (84.8%)	3.53 (1.31, 9.48)	
Sex				.594
Female	26 (26.8%)	71 (73.2%)	1.19 (0.63, 2.25)	
Male	27 (30.3%)	62 (69.7%)	1.00 (– –)	
Race				.284
Black	14 (23.3%)	46 (76.7%)	1.47 (0.73, 2.99)	
Non-Black	39 (31.0%)	87 (69.0%)	1.00 (– –)	
Baseline mRS				.038
0–1	47 (32.2%)	99 (67.8%)	1.00 (– –)	
2–3	6 (15.0%)	34 (85.0%)	2.69 (1.06, 6.85)	
GCS, median (IQR)		-	0.65 (0.54, 0.79)	<.001
Initial NIHSS				<.001
≤ 11 (median)	48 (49.5%)	49 (50.5%)	1.00 (– –)	
> 11	5 (5.6%)	84 (94.4%)	16.46 (6.14, 44.11)	
ICH volume (mL)				<.001
Q1 (0–6.0)	23 (46.9%)	26 (53.1%)	1.00 (– –)	
Q2 (6.1–18.6)	16 (36.4%)	28 (63.6%)	1.55 (0.67, 3.56)	
Q3 (18.7–43.3)	12 (25.5%)	35 (74.5%)	2.58 (1.09, 6.12)	
Q4 (43.4–130.6)	2 (4.3%)	44 (95.7%)	19.46 (4.24, 89.35)	
Subarachnoid extension				.016
Yes	2 (7.1%)	26 (92.9%)	6.20 (1.42, 27.12)	
No	51 (32.3%)	107 (67.7%)	1.00 (– –)	
Intraventricular extension				<.001
Yes	17 (16.3%)	87 (83.7%)	4.01 (2.03, 7.89)	
No	36 (43.9%)	46 (56.1%)	1.00 (– –)	
Supratentorial				.799
Yes	48 (28.2%)	122 (71.8%)	1.15 (0.38, 3.50)	
No	5 (31.2%)	11 (68.8%)	1.00 (– –)	

	mRS 0–3 (N = 53)	mRS 4–6 (N = 133)	Unadjusted OR (95% CI) for predicting mRS 4–6	p-value
	N (%)	N (%)		
Lobar				.187
Yes	30 (33.0%)	61 (67.0%)	1.00 (– –)	
No	23 (24.2%)	72 (75.8%)	1.54 (0.81, 2.92)	
Initial SBP, mmHg				.605
Q1 (107–156)	15 (31.2%)	33 (68.8%)	1.00 (– –)	
Q2 (157–182.5)	17 (33.3%)	34 (66.7%)	0.91 (0.39, 2.1)	
Q3 (182.6–211)	9 (21.4%)	33 (78.6%)	1.67 (0.64, 4.34)	
Q4 (212–282)	12 (26.7%)	33 (73.3%)	1.25 (0.51, 3.07)	
Initial DBP, mmHg				.652
Q1 (47–86)	12 (25.5%)	35 (74.5%)	1.00 (– –)	
Q2 (87–100)	18 (34.6%)	34 (65.4%)	0.65 (0.27, 1.55)	
Q3 (101–112)	12 (29.3%)	29 (70.7%)	0.83 (0.32, 2.12)	
Q4 (113–183)	11 (23.9%)	35 (76.1%)	1.09 (0.43, 2.80)	
Charlson				.566
0–1	37 (29.8%)	87 (70.2%)	1.00 (– –)	
>1	16 (25.8%)	46 (74.2%)	1.22 (0.62, 2.43)	
Craniotomy				.717
Yes	8 (25.8%)	23 (74.2%)	1.18 (0.49, 2.82)	
No	45 (29.0%)	110 (71.0%)	1.00 (– –)	
Prior ICH				.782
Yes	8 (33.8%)	18 (69.2%)	1.00 (– –)	
No	45 (28.1%)	115 (71.9%)	1.14 (0.46, 2.80)	
Prior ischemic stroke				.146
Yes	4 (16.0%)	21 (84.0%)	2.30 (0.75, 7.04)	
No	49 (30.4%)	112 (69.6%)	1.00 (– –)	
Prophylactic anticonvulsant				.417
Yes	24 (25.8%)	69 (74.2%)	1.30 (0.69, 2.47)	
No	29 (31.2%)	64 (68.8%)	1.00 (– –)	

Table 5:

Predictors of poor outcome (mRS 4–6) at hospital discharge

Model	OR (95% CI)	p-value
Prophylactic anticonvulsant		.424
Yes	1.41 (0.61, 3.29)	
No	1.00 (– –)	
Initial NIHSS		<.001
≤ 11 (median)	1.00 (– –)	
>11	13.95 (4.80, 40.50)	
ICH volume (mL)		.007
Q1 (0–6.0)	1.00 (– –)	
Q2 (6.1–18.6)	2.02 (0.72, 5.66)	
Q3 (18.7–43.3)	2.24 (0.73, 6.84)	
Q4 (43.4–130.6)	19.28 (3.58, 103.71)	
Intraventricular extension		.006
Yes	3.33 (1.41, 7.88)	
No	1.00 (– –)	
Baseline mRS		.008
0–1	1.00 (– –)	
2–3	5.05 (1.53, 16.66)	