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]

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

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

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Search terms: intracerebral hemorrhage, outcomes, anticonvulsants, health services, guideline adherence

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.

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.

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.

<u>Cohort assembly</u>

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.

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Conflict of Interest/Disclosures

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Table 1: Univariate logistic regression for prophylactic anticonvulsant (PA) administration

	Not Prescribed PA (N = 408)	Prescribed PA (N = 98)	Unadjusted OR (95% CI) for predicting PA	p-value
	N (%)	N (%)		
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)	

	Not Prescribed PA (N = 408)	Prescribed PA (N = 98)	Unadjusted OR (95% CI) for	p-value
	N (%)	N (%)	predicting PA	
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 (– –)	
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 (– –)	
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, 2.11)	
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)	

	mRS 0-3 (N = 53)	mRS 4-6 (N = 133)	Unadjusted OR (95% CI) for predicting mRS 4-6	p-value
	N (%)	**N (%)**		
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)	