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Medication History versus Point-of-Care Platelet Activity Testing in Patients with Intracerebral Hemorrhage

Matthew B. Maas, MD, Andrew M. Naidech, MD, MSPH, Minjee Kim, MD, Ayush Batra, MD, Edward M. Manno, MD, MS, Farzaneh A. Sorond, MD, PhD, Shyam Prabhakaran, MD, MS, and Eric M. Liotta, MD

Division of Stroke and Critical Care, Department of Neurology, Northwestern University, Chicago, IL

Abstract

Objective—We evaluated whether reduced platelet activity detected by point-of-care (POC) testing is better predictor of hematoma expansion and poor functional outcomes in patients with intracerebral hemorrhage (ICH) than a history of antiplatelet medication exposure.

Methods—Patients presenting with spontaneous ICH were enrolled in a prospective observational cohort study that collected demographic, clinical, laboratory, and radiographic data. We measured platelet activity using the PFA-100 (Siemens AG, Germany) and VerifyNow-ASA (Accumetrics, CA, USA) systems on admission. We performed univariate and adjusted multivariate analyses to assess the strength of association between those measures and 1) hematoma growth at 24 hours and 2) functional outcomes measured by the modified Rankin Scale (mRS) at 3 months.

Results—We identified 278 patients for analysis (mean age 65 ± 15 , median ICH score 1 [interquartile range 0–2]), among whom 164 underwent initial neuroimaging within 6 hours of symptom onset. Univariate association with hematoma growth was stronger for antiplatelet medication history than POC measures, which was confirmed in multivariable models (β 3.64 [95% CI 1.02–6.26], $p=0.007$), with a larger effect size measured in the < 6 -hour subgroup (β 7.20 [3.35–11.1], $p<0.001$). Moreover, antiplatelet medication history, but not POC measures of platelet activity, was independently associated with poor outcome at 3 months (mRS 4–6) in the < 6 -hour subgroup (adjusted OR 3.6 [1.2–11], $p=0.023$).

Conclusions—A history of antiplatelet medication use better identifies patients at risk for hematoma growth and poor functional outcomes than POC measures of platelet activity after spontaneous ICH.

Corresponding Author: Dr. Matthew Maas, 710 N Lake Shore Drive, 11th Floor, Dept of Neurology, Chicago, IL 60611, Phone: 312-503-0479, Fax: 312-908-5073, mbmaas@northwestern.edu.

Conflict of Interest:

All authors declare that they have no conflict of interest.

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Keywords

intracerebral hemorrhage; intracranial hemorrhage; hemorrhagic stroke; hemostasis; platelet dysfunction; antiplatelet

Introduction

Antiplatelet medication exposure and reduced platelet activity detected using point-of-care (POC) tests have been associated with worse functional outcomes and greater mortality in patients with spontaneous intracerebral hemorrhage (ICH).(1–5) Similar to anticoagulant exposure, platelet dysfunction is believed to mediate harm through hematoma expansion.(6, 7) Although platelet dysfunction imparts less risk of harm than anticoagulants, approximately a quarter of all ICH patients report pre-treatment with antiplatelet medications.(1) Few therapeutic options exist to improve outcomes after ICH, so platelet dysfunction is a therapeutic target of interest.(8, 9)

Individual patient responses to antiplatelet medications are variable, with a considerable proportion exhibiting diminished or absent antiplatelet effects.(10, 11) Moreover, POC platelet activity screening in patients with acute ICH has found that 24% of cases with no discernible history of antiplatelet medication exposure show reduced platelet activity, suggesting that medication history may be an inaccurate identifier of exposure.(6) As a result, it is not known which approach, POC testing or eliciting medication history, is superior for identification of patients at risk for platelet dysfunction related morbidity after ICH, or whether they may be complementary. The objective of this study was to determine whether reduced platelet activity detected by POC testing is more strongly associated with hematoma expansion at 24 hours and poor functional outcomes at 3 months than a history of antiplatelet medication exposure.

Methods

Patients presenting to Northwestern Memorial Hospital with spontaneous ICH between January 2010 and March 2016 were prospectively enrolled in an observational cohort study. All cases were diagnosed by a board-certified vascular neurologist or neurointensivist utilizing CT and/or MR imaging. Patients with ICH attributed to trauma, hemorrhagic conversion of ischemic stroke, structural lesions or vascular malformations were excluded. All patients were admitted to a neuro/spine-intensive care unit (NSICU) with a standard order set in the electronic order entry system. The Glasgow Coma Scale (GCS) score was prospectively recorded at the time of initial evaluation by a trained neurologist and/or neurosurgeon. Our protocol included at least one repeat non-contrast head CT, generally after 24 hours, to assess for hematoma growth, as previously reported in detail.(12)

Demographic information, medical history, medication history, standardized clinical instruments (GCS, pre-ICH modified Rankin Scale [mRS]), pretreatment blood pressure, laboratory data, imaging data, medical management variables, surgical interventions and medical complications were prospectively recorded. Hematoma volumes were measured on industry standard DICOM images using Analyze software (Mayo Clinic, Rochester, MN)

with a semi-automated process, a technique with high reliability that has been used as an endpoint in other ICH studies.(13) We routinely measured platelet activity by POC testing using both the PFA-100 (Siemens AG, Germany) and the VerifyNow-ASA (Accumetrics, CA, USA) systems on admission. We used the PFA-EPI measurement from the PFA-100 system and aspirin reaction units (ARU) from the VerifyNow system as previously described.(6, 14) ARU 550 indicates reduced platelet activity in the range of therapeutic aspirin medication effect.(6) Medication history, including over-the-counter medications, was obtained by a critical care pharmacist through mandated medication reconciliation by interviewing the patient and/or their family, and contacting outpatient pharmacies as previously reported.(14) Because initial laboratory data was not uniformly available for patients transferred to our institution from another facility, this study included only patients who presented initially to our hospital. Likewise, patients were excluded if a repeat non-contrast head CT was unavailable to measure hematoma volume change, as well as patients in whom platelet function testing was not performed.

After evaluating continuous variables for distribution characteristics, we determined that hematoma volume change from initial CT to first repeat CT imaging was normally distributed and appropriate for linear regression modeling. We built a fully adjusted multivariate model by initially including clinical variables that were associated with hematoma growth by univariate testing. We then used a stepwise elimination approach to create a parsimoniously adjusted model with less susceptibility to overfitting, and observed whether POC platelet activity measurements or antiplatelet use history was preferentially retained in the adjusted model. Next, we analyzed outcomes using the 3-month mRS adjusted for age, admission GCS, and initial hematoma volume. After determining that the data did not fulfill the proportional odds assumption for ordinal regression modeling as assessed by the test of parallel lines, we dichotomized the mRS treating 0–3 as good outcome and 4–6 as poor outcome, and used a binary logistic regression model. Given that the mechanism of harm from platelet dysfunction is hypothesized to be mediated through hematoma growth, we separately performed the same analyses on the subgroup of patients who presented early enough to undergo initial head CT within 6 hours of symptom onset, as these patients are at highest risk for observable hematoma growth. As exploratory secondary analyses, we sought to identify possible confounding due to warfarin exposure, platelet transfusions and desmopressin use first by repeating the models for hematoma growth excluding all patients with a history of warfarin exposure, and then adding terms of platelet transfusion and desmopressin treatment to the initial model and repeating the stepwise selection process. The statistical analyses was performed in R version 3.4.0.

The study was approved by the Institutional Review Board (IRB). Written informed consent was obtained from the patient or their legally authorized representative. The IRB approved a waiver of consent for patients who died during initial hospitalization, or who were incapacitated and for whom a legal representative could not be located.

Results

We included 278 patients (mean 65 ± 15 years old, 51% female, 51% white) with requisite data for analysis. Anticoagulant use was uncommon as reflected by low reported warfarin

use (9%) and admission coagulation testing (median international normalized ratio 1.1 [1.0–1.2]), although 106 patients (38%) reported antiplatelet medication use. Platelet function testing showed a wide range of platelet activity (median ARU 567 [470–641] and PFA-EPI 147 [111–228] seconds), with 108 (43%) patients found to have reduced platelet activity in the range therapeutic aspirin effect (ARU $\leq$ 550). Among the 108 patients measured as having therapeutic intensity ARU, medication history was ascertained in all but one, and 43 (40%) reported no antiplatelet medication use. The relationship between ARU and aspirin use history is shown as distribution densities in Figure 1. A more complete summary of the patients' demographic and clinical characteristics is shown in Table 1. There were 164 patients who presented early enough to undergo initial head CT within 6 hours of symptom onset (“ < 6 -hour subgroup”).

ARU was not correlated with hematoma volume change in the complete cohort (Spearman correlation $p=0.20$) but was in the < 6 -hour subgroup (Spearman's rho -0.18 , $p=0.027$). PFA-EPI was not correlated with hematoma volume change in either the complete cohort or the < 6 -hour subgroup ($p=0.31$ and $p=0.4$, respectively). Mean hematoma change was greater in patients with a history of antiplatelet medication use than those without in the complete cohort (mean 3.2 mL versus 0.8 mL, $p=0.037$) as well as within the < 6 -hour subgroup (mean 5.0 mL versus 0.7 mL, $p=0.028$).

Multivariable modeling of hematoma volume change showed that antiplatelet medication history was retained as a predictor preferentially over POC platelet activity (measured in ARU or PFA-EPI) in both the complete cohort and < 6 -hour subgroup, and remained an independent predictor of hematoma growth in the final models for both groups. As expected, the relationship between antiplatelet medication exposure and hematoma growth was stronger in the < 6 -hour subgroup (β 7.20 [95%CI 3.35–11.1], $p<0.001$), with nearly double the estimated effect size compared to the complete cohort (β 3.64 [1.02–6.26], $p=0.007$). The results of the hematoma volume change analyses are shown in Table 2. Repeat analysis excluding patients with a history of warfarin use yielded similar effect sizes and significance (antiplatelet medication effect in complete cohort β 3.75 [1.13–6.37], $p=0.005$ and in the < 6 hour cohort β 7.09 [3.31–10.9], $p<0.001$). Similarly, a secondary analysis to probe the potential effect of platelet transfusion and desmopressin treatment on hematoma growth, each of which was given to a limited minority of patients, showed no significant effect and those terms were removed from the model.

In the complete cohort, neither platelet activity measurements by POC nor antiplatelet medication use were associated with 3-month functional outcomes after adjustment for age, initial GCS and initial hematoma volume. However, antiplatelet medication use, but not platelet activity by POC, was independently associated with poor outcome (mRS 4–6) in the < 6 -hour subgroup (adjusted OR 3.6 [1.2–11], $p=0.023$) as summarized in Table 3.

In order to better understand the potential significance of diminished POC platelet activity in patients with no history of antiplatelet medication use, we performed two analyses. First, we created a model of hematoma growth using only patients with platelet activity that was reduced to a therapeutic range (ARU $\leq$ 550), and found that a history of antiplatelet medication use, but not ARU, was independently associated with hematoma volume change

in the complete cohort (β 6.74 [2.43–11.05], $p=0.003$) and in the < 6 -hour subgroup (β 11.5 [5.34–17.69], $p<0.001$). Second, we evaluated the subgroup of patients with no history of antiplatelet medication use and found that neither POC measure of platelet activity (ARU or PFA-EPI) was independently associated with hematoma growth in either the full cohort or the < 6 -hour subgroup.

Discussion

In this observational cohort of patients with spontaneous ICH, we found that antiplatelet medication use history is more strongly associated with hematoma growth than POC derived measures of platelet activity. Furthermore, history of antiplatelet medication use, but not measured POC platelet activity, was independently associated with poor functional outcome in the high-risk subgroup of patients presenting within 6 hours of symptom onset. The finding that the risk estimates linking antiplatelet medication use with hematoma growth and functional outcomes were greater in the < 6 -hour patients supports the hypothesis that antiplatelet medications mediate poor outcomes through impaired hemostasis that promotes hematoma growth. We replicated a previously reported finding that a substantial proportion of patients with reduced platelet activity have no history of antiplatelet medication use, but found no evidence that the abnormal POC finding was associated with increased risk of hematoma growth, whereas a history of antiplatelet medication use identified elevated risk regardless of POC platelet activity measurements. Secondary analyses to look for effects from warfarin exposure, platelet transfusions and desmopressin treatment, all of which were relevant to a small minority of the patients, found no effect of those variables on the relationship between our measures of platelet dysfunction and hematoma growth. We conclude that POC platelet activity testing offers no complementary discriminatory value to ascertaining medication exposure.

Although many groups have ascertained antiplatelet medication use history and reported those findings, there are limited reports of laboratory measurements of platelet activity in patients with ICH.(1) Our institution has routinely obtained POC platelet function testing in patients with intracranial bleeding, including patients with ICH. We have previously reported associations between the reduced platelet activity and more intraventricular hemorrhage, hematoma growth, likelihood of craniotomy, and poor outcomes in patients with ICH.(15–17) Those prior studies were based on substantially smaller sized cohorts such that the power to compare platelet function testing and antiplatelet use history was limited. We did observe that approximately 40% of patients in our early studies with abnormal platelet activity measurements had no history of antiplatelet medication exposure, which remained a consistent finding now with nearly four times the number of patients studied.(14) The significance of reduced platelet activity on POC testing in the absence of antiplatelet medication exposure was heretofore unknown, but is shown in these data to be clinically unimportant with respect to hematoma growth and outcomes. Moreover, we included initial magnesium in the hematoma growth models in light of recent findings that there is a link between magnesium, ICH growth and functional outcomes.(18)

Recent systematic reviews of POC platelet function testing report that the reliability of these tests is unsatisfactory, and in patients with ICH, agreement between different POC platelet

function assays is reported to be poor.(11, 14, 19) Consistent with findings in the cardiovascular literature, although associations between important clinical measures and POC platelet activity tests are measurable in this cohort, the associations are weaker and less informative than determining antiplatelet medication exposure by history. As shown in Figure 1, POC platelet activity tests have poor agreement with medication use history. Our results suggest that current POC techniques to measure physiologically meaningful in vivo antiplatelet medication effects are suboptimal. Platelet activity measures have been shown to change in response to platelet transfusions and desmopressin in patients with acute ICH. Therefore, although absolute platelet activity levels are less useful, POC testing may find future application as a biomarker of treatment efficacy, as well as in cases where a medication history cannot be readily obtained.(9, 20)

There are limitations to this study. These data are drawn from a single center cohort, and as such may be susceptible to biases related to our institutional practices and the clinical and sociodemographic profile of patients we see. Moreover, the two POC systems we tested may not represent the performance of other in vitro platelet function testing systems. The pathologic influence of antiplatelet agents in ICH is also not firmly established. Although most groups who have examined the relationship between antiplatelet medications and ICH outcomes have reported a significant, harmful association, other studies have failed to replicate those findings.(1, 21) We performed secondary analyses to evaluate potential confounding by warfarin exposure, platelet transfusions and desmopressin treatment and identified no meaningful effects, although it is possible that a larger study could identify more modest effects of those variables, or other conditions like uremia for which we did not have sufficient observations to evaluate. The data we present here showing an association with hematoma growth and functional outcomes lends weight to the hypothesis that an important, causal relationship is present. Finally, given that routine POC platelet activity testing is not widely performed in patients with ICH, accruing a large, multicenter cohort is challenging.

Conclusion

Given the large proportion of patients with ICH who have antiplatelet medication exposure and the association with poor outcomes, platelet dysfunction merits attention, and determining the most useful method of characterizing patients' risk exposure is of fundamental importance. Although an association is observable between POC measured platelet activity and hematoma growth, antiplatelet medication use history is a superior marker of exposure, and is also independently predictive of functional outcomes. Moreover, reduced platelet activity by POC testing is found to have no association with hematoma growth apart from antiplatelet medication exposure. While POC platelet function testing may be helpful in limited cases where medication history is unknown, or as a biomarker to monitor therapeutic interventions, carefully obtaining a medication history to screen for antiplatelet medication use may be simpler and superior to POC testing.

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References

1. Thompson BB, Béjot Y, Caso V, et al. Prior antiplatelet therapy and outcome following intracerebral hemorrhage: A systematic review. *Neurology*. 2010; 75:1333–1342. [PubMed: 20826714]
2. Naidech AM, Kumar MA. Monitoring of hematological and hemostatic parameters in neurocritical care patients. *Neurocritical Care*. 2014; 21(Suppl 2):S168–76. [PubMed: 25208669]
3. Naidech AM, Bernstein RA, Levasseur K, et al. Platelet activity and outcome after intracerebral hemorrhage. *Ann Neurol*. 2009; 65:352–356. [PubMed: 19334079]
4. Saloheimo P, Ahonen M, Juvela S, Pyhtinen J, Savolainen ER, Hillbom M. Regular aspirin-use preceding the onset of primary intracerebral hemorrhage is an independent predictor for death. *Stroke*. 2006; 37:129–133. [PubMed: 16322483]
5. Creutzfeldt CJ, Weinstein JR, Longstreth WT Jr, Becker KJ, McPharlin TO, Tirschwell DL. Prior antiplatelet therapy, platelet infusion therapy, and outcome after intracerebral hemorrhage. *J Stroke Cerebrovasc Dis*. 2009; 18:221–228. [PubMed: 19426894]
6. Naidech AM, Jovanovic B, Liebling S, et al. Reduced platelet activity is associated with early clot growth and worse 3-month outcome after intracerebral hemorrhage. *Stroke*. 2009; 40:2398–2401. [PubMed: 19443791]
7. Broderick JP, Diringer MN, Hill MD, et al. Determinants of intracerebral hemorrhage growth: An exploratory analysis. *Stroke*. 2007; 38:1072–1075. [PubMed: 17290026]
8. Roquer J, Hidalgo RMV, Ois A, et al. Antithrombotic pretreatment increases very-early mortality in primary intracerebral hemorrhage. *Neurology*. 2017; 88:885–891. [PubMed: 28148636]
9. Naidech AM, Maas MB, Levasseur-Franklin KE, et al. Desmopressin improves platelet activity in acute intracerebral hemorrhage. *Stroke*. 2014; 45:2451–2453. [PubMed: 25005444]
10. Sweeny JM, Gorog DA, Fuster V. Antiplatelet drug ‘resistance’ part 1: Mechanisms and clinical measurements. *Nat Rev Cardiol*. 2009; 6:273–282. [PubMed: 19352331]
11. Harrison P, Segal H, Blasbery K, Furtado C, Silver L, Rothwell PM. Screening for aspirin responsiveness after transient ischemic attack and stroke: Comparison of 2 point-of-care platelet function tests with optical aggregometry. *Stroke*. 2005; 36:1001–1005. [PubMed: 15817896]
12. Maas MB, Rosenberg NF, Kosteva AR, et al. Surveillance neuroimaging and neurologic examinations affect care for intracerebral hemorrhage. *Neurology*. 2013; 81:107–112. [PubMed: 23739227]
13. Maas MB, Nemeth AJ, Rosenberg NF, Kosteva AR, Prabhakaran S, Naidech AM. Delayed intraventricular hemorrhage is common and worsens outcomes in intracerebral hemorrhage. *Neurology*. 2013; 80:1295–1299. [PubMed: 23516315]
14. Naidech AM, Bassin SL, Bernstein RA, Batjer HH, Alberts MJ, Lindholm PF, Bleck TP. Reduced platelet activity is more common than reported anti-platelet medication use in patients with intracerebral hemorrhage. *Neurocrit Care*. 2009; 11:307–310. [PubMed: 19381881]
15. Naidech AM, Jovanovic B, Liebling S, et al. Reduced platelet activity is associated with early clot growth and worse 3-month outcome after intracerebral hemorrhage. *Stroke*. 2009; 40:2398–2401. [PubMed: 19443791]
16. Naidech AM, Bendok BR, Garg RK, Bernstein RA, Alberts MJ, Bleck T, Batjer HH. Reduced platelet activity is associated with more intraventricular hemorrhage. *Neurosurgery*. 2009; 65:684–8. discussion 688. [PubMed: 19834372]
17. Naidech AM, Rosenberg NF, Bernstein RA, Batjer HH. Aspirin use or reduced platelet activity predicts craniotomy after intracerebral hemorrhage. *Neurocrit Care*. 2011; 15:442–446. [PubMed: 21567303]

18. Liotta EM, Prabhakaran S, Sangha RS, et al. Magnesium, hemostasis, and outcomes in patients with intracerebral hemorrhage. *Neurology*. 2017; 89:813–819. [PubMed: 28747450]
19. Gorog DA, Sweeny JM, Fuster V. Antiplatelet drug ‘resistance’. part 2: Laboratory resistance to antiplatelet drugs—fact or artifact? *Nat Rev Cardiol*. 2009; 6:365–373. [PubMed: 19365406]
20. Naidech AM, Liebling SM, Rosenberg NF, et al. Early platelet transfusion improves platelet activity and may improve outcomes after intracerebral hemorrhage. *Neurocrit Care*. 2012; 16:82–87. [PubMed: 21837536]
21. Sansing LH, Messe SR, Cucchiara BL, Cohen SN, Lyden PD, Kasner SE. Prior antiplatelet use does not affect hemorrhage growth or outcome after ICH. *Neurology*. 2009; 72:1397–1402. [PubMed: 19129506]

Figure 1.
Distribution Density of ARU by Aspirin Dose History

Table 1**Patient Characteristics**

Age (yr)	65 ± 15
Gender (female)	143 (51%)
Race	
Unknown/Other	1 (0.4%)
American Indian/Native Alaskan	1 (0.4%)
Asian	6 (2%)
Black or African-American	118 (42%)
Native Pacific Islander	9 (3%)
White	143 (51%)
Hispanic ethnicity	20 (7%)
Admit GCS	14 [10–15]
ICH Score	1 [0–2]
Initial hematoma volume (mL)	8.7 [3.4–21.2]
Intraventricular hemorrhage on presentation	107 (39%)
Lobar location	101 (37%)
Warfarin	26 (9%)
Novel Oral Anticoagulant	2 (0.7%)
Low Molecular Weight Heparin	3 (1%)
Antiplatelet medication	106 (38%)
Aspirin monotherapy	84 (30%)
Other antiplatelet medication monotherapy	8 (3%)
Dual antiplatelet therapy	14 (5%)
Initial INR	1.1 [1.0–1.2]
Initial platelet count ($\times 10^9/L$)	238 ± 81
Initial platelet function measured by aspirin resistance units (ARU)	567 [470–641]
Initial platelet function measured by PFA-EPI	147 [111–228]
ARU 550	108 (43%)
Platelet dysfunction treatments:	
Platelet transfusion	53 (19%)
Desmopressin	30 (11%)
Platelet transfusion and desmopressin	10 (4%)
Time from symptom onset to initial CT (hr)	3.2 [1.1–13.1]
Time between initial and follow up CT (hr)	24.3 [11.0–36.0]
Change in hematoma volume (ml)	0.1 [−0.9–1.9]
Modified Rankin Scale score at 1 month	4 [3–5]
Modified Rankin Scale score at 3 months	4 [2–6]

Table 2

Linear Regression Models for Hematoma Growth

Clinical Variables	Univariate Unadjusted			Fully Adjusted Model			Parsimonious Model		
Hematoma Volume Change for All Patients									
	β	SE	p	β	SE	p	β	SE	p
Antiplatelet use	2.38	1.14	0.037	3.93	1.55	0.012	3.64	1.33	0.007
Aspirin reaction units (ARU)	−0.04	0.006	0.46	0.001	0.008	0.86	--	--	--
PFA-EPI	0.000	0.008	0.97	−0.005	0.010	0.61	--	--	--
Initial platelet count (×10 ⁹ /L)	--	--	--	0.016	0.009	0.058	0.017	0.008	0.036
Age (years)	--	--	--	−0.102	0.051	0.046	−0.087	0.046	0.057
Time interval between CT scans	--	--	--	−2.40	0.91	0.009	−2.20	0.87	0.012
Initial magnesium (Mg)	--	--	--	−5.85	2.55	0.023	−6.71	2.42	0.006
International normalized ratio (INR)	--	--	--	−0.31	1.26	0.81	--	--	--
Initial systolic blood pressure (SBP)	--	--	--	−0.025	0.017	0.15	--	--	--
Lobar hematoma location	--	--	--	−1.96	1.55	0.21	--	--	--
Initial hematoma volume	--	--	--	1.11	0.94	0.24	--	--	--
Time from onset to initial CT	--	--	--	−0.82	0.64	0.20	--	--	--
Hematoma Volume Change for Patients Presenting Within 6 Hours									
	β	SE	p	β	SE	p	β	SE	p
Antiplatelet use	4.30	1.74	0.014	6.88	2.24	0.003	7.20	1.95	<0.001
Aspirin reaction units (ARU)	−0.013	0.009	0.13	−0.005	0.011	0.68	--	--	--
PFA-EPI	−0.005	0.011	0.67	−0.007	0.014	0.63	--	--	--
Initial platelet count (×10 ⁹ /L)	--	--	--	0.023	0.013	0.074	0.025	0.011	0.028
Age (years)	--	--	--	−0.17	0.077	0.026	−0.19	0.072	0.011
Time interval between CT scans	--	--	--	−2.99	1.35	0.029	−2.66	1.25	0.036
Initial magnesium (Mg)	--	--	--	−7.60	3.63	0.039	−8.30	3.41	0.016
International normalized ratio (INR)	--	--	--	−0.30	2.05	0.88	--	--	--
Initial systolic blood pressure (SBP)	--	--	--	−0.030	0.026	0.24	--	--	--

Clinical Variables	Univariate Unadjusted			Fully Adjusted Model			Parsimonious Model		
Hematoma Volume Change for All Patients									
	β	SE	p	β	SE	p	β	SE	p
Lobar hematoma location	--	--	--	-3.43	2.35	0.15			
Initial hematoma volume	--	--	--	1.18	1.25	0.35			
Time from onset to initial CT	--	--	--	0.050	18.28	0.998			

Table 3

Binary Logistic Regression Models for Functional Outcomes

Poor Outcome at 3 Months (mRS 4–6) for Patients Presenting Within 6 Hours						
	Model Using Platelet Activity Testing		Model Using Antiplatelet Medication History			
	Exp(β)	95% CI	p	Exp(β)	95% CI	p
Aspirin reaction units (ARU)	1.00	0.99–1.004	0.37	--	--	--
Antiplatelet medication use	--	--	--	3.30	1.1–11.1	0.044
Age (years)	1.02	0.98–1.07	0.31	1.02	0.98–1.06	0.42
Admission GCS	0.65	0.53–0.78	<0.001	0.63	0.50–0.76	<0.001
Initial hematoma volume	1.06	1.02–1.11	0.013	1.06	1.02–1.11	0.018