

Rate of hematoma expansion as a predictor of outcome in intracerebral hemorrhage

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Abstract

Objective: We examined the association between intracerebral hemorrhage hematoma expansion rate and 90-day outcomes using the Qatar Stroke Registry. **Methods:** We conducted a retrospective analysis of patients admitted with supratentorial intracerebral hemorrhage from January 2014 to December 2024. The modified Rankin Scale was dichotomized into favourable (0–3) and unfavourable outcomes (4–6). **Results:** A total of 1,351 patients were included in the final analysis. Fast volume-expanders (>10 mL/hr) had the highest mRS ($p=0.002$) and highest proportion of mortality at 90 days, compared to the slow volume expander (<5 mL/hr) and intermediate volume expander (5–10 mL/hr), $p=0.01$. Multivariate analysis revealed that severe NIHSS admission score (>10) was an independent predictor of mortality at 90 days (aOR 11.4, 95% CI: 4.58–28.5). Fast hematoma expansion rate was marginally associated with mortality at 90 days (aOR: 1.79, 95% CI: 0.99–3.20). In contrast, age (aOR 1.03, 95% CI: 1.02–1.04, $p<.001$), moderate stroke (aOR 3.21, 95% CI: 1.79–5.75, $p<.001$), severe stroke (aOR 27.0, 95% CI: 15.9–45.9, $p<.001$), and fast hematoma expansion rate (aOR 1.77, 95% CI: 1.10–2.85, $p=0.02$) were identified as predictors of a poor outcome (mRS of 4–6) at 90 days.

Conclusion: Fast hematoma expansion is independently associated with worse 90-day outcomes in the Arab population. In resource-limited settings where access to computed tomography angiography might be limited, using a CT head to calculate the volume expansion rate could be a useful predictor of outcomes in patients with supratentorial ICH.

Keywords: Intracerebral hemorrhage, hematoma, CT, volume expansion

INTRODUCTION

Intracerebral hemorrhage (ICH) has high rates of morbidity and mortality.^{1,2} The overall case fatality rate for ICH at one month is 40% and 46.7–63.6% at one year post-index event.³ The estimated disability-adjusted-life-years (DALYs) and years of life lost (YLL) to a single ICH event are 9.46 and 5.72, respectively.⁴ Several studies have reported that hematoma expansion is a significant predictor of ICH outcomes, with a 10% increase in ICH growth leading to a 18% decline in independence.^{5,6} The definition of a clinically significant hematoma expansion is still not universally defined due to the variable classification of volume increases across studies.⁷ Moreover, several factors are associated with ICH expansion, such as volume of ICH at baseline, antithrombotic drugs use, contrast imaging

markers, and time from symptom onset to initial imaging.⁷ Although the initial hematoma volume is a well-recognized predictor of mortality in patients with ICH^{8,9}, little is known about hematoma expansion rate (defined as the ratio of baseline hematoma volume and time from onset to imaging acquisition) in predicting ICH patient outcomes. The objective of this study is to determine the association between hematoma expansion rate and patient outcomes using the Qatar Stroke Registry.

METHODS

Data from patients admitted with a stroke to Hamad General Hospital (HGH), Doha, Qatar from January 2014 through December 2024 were retrospectively analyzed from a hospital based prospective stroke registry. We studied patients

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with acute primary supratentorial ICH. We excluded those with infratentorial bleeds (bleeds from the brain stem, cerebellum, and primary ventricular) or had missing initial hematoma volume. We also excluded patients with ICH secondary to cerebral aneurysms, arteriovenous malformations, infections or brain tumors. There were 1,660 ICH patients entered into the registry of whom 1,351 patients met our inclusion criteria and were included in the final analysis.

Patient characteristics

Patient characteristics including age, sex, nationality, medical comorbidities and prior medication were collected in the Stroke Registry. Data from the NIH Stroke Scale (NIHSS) score, neuroimaging data, post-discharge disposition were entered into the registry. Ischemic stroke was diagnosed according to the WHO criteria¹⁰ and stroke subtypes by the TOAST criteria. The modified Rankin scale (MRS) was measured at discharge and at 90 days following onset of symptoms. The patient-outcomes were classified as favourable (mRS \leq 0-3) or unfavourable (mRS 4-6) outcome. We used the dichotomized mRS scale as it is the most common method in use to evaluate recovery at 90 days.

Data collection

Upon identification and confirmation of diagnosis using the International Classification of Disease, 10th edition, definitions (H34.1, 163.x, 164.x, 161.x, 160.x, G45.x), patients' data were collected by trained stroke coordinators. The ethnicities of the patients were recorded at admission. Written informed consent was not required to participate in this study as it is a retrospective analysis.

Radiological variables

Patients' head CT scans were analyzed to identify the following data: location (basal ganglia, brainstem, cerebellum, cortical, or thalamus), ICH volume (cm³) measured using the method with the largest length in three dimensions divided by two (equation: $ABC/2$); presence or absence of intraventricular hemorrhage (IVH). We did not use any cut-offs for the size of the hematoma in the study population.

Volume expansion definition

In our study, we categorized our time from onset of symptoms to CT imaging into three groups: <2 hours, 2-6 hours and >6 hours. Based on

the patient's onset duration, we then took their baseline hematoma volume and divided it by a factor of 2 (for patients with an onset duration of <2 hours), 3 (for patients with an onset duration between 2 to 6 hours), and 6 (for patients with an onset duration of greater than 6 hours). After we obtained this value, we then categorized the volume expansion rate into three categories: 1) <5 mL/hr (slow-volume expander), 2) 5-10 mL/hr (intermediate volume expander) and 3) >10 mL/hr (fast volume expander). We also conducted a separate analysis for a volume expansion rate of <1 mL/hr, 1-11 mL/hr and >11 mL/hr and <2 mL/hr, 2-10 mL/hr and >10 mL/hr. However, hematoma expansion rate was not a significant independent predictor for a higher mRS at 90 days and mortality at 90 days, therefore we went with the hematoma expansion rate of <5 mL/hr, 5-10 mL/hr and >10 mL/hr for this paper.

Statistical analysis

Descriptive results for all continuous variables were reported as mean \pm standard deviation (SD) for normally distributed data or median with range for data with non-normal distributions. The distribution of continuous variables was assessed before using statistical tools. Mean level comparisons between patients with slow, intermediate, and fast hematoma expansion were assessed using ANOVA test and multiple comparisons were performed using Bonferroni correction. If an assumption of an ANOVA test was failed, then an alternative non-parametric Kruskal Wallis test was performed, followed by Dunn's post-hoc test. Pearson Chi-Square test and Fisher's Exact test were performed whenever appropriate to compare the proportion of all categorical variables between the groups. Multiple logistic regression analysis was performed to assess for risk factors associated with a higher mRS at 90 days (4-6) and mortality at 90 days after selecting important and significant variables at univariate analysis. Odds ratio (OR) and the 95% confidence interval for the OR were reported. A p-value of ≤ 0.05 (two-tailed) was considered significant. Stata version 18.5 for Mac was used for the analysis.

RESULTS

In total, there were 963 patients in the slow volume expander group (<2 mL/hr), 180 patients in the intermediate volume expander group (2-10 mL/hr) and 117 patients in the fast volume expander group (>10 mL/hr). There were no significant

differences between the three volume expansion groups in terms of age ($p=0.61$), gender ($p=0.56$), smoking status ($p=0.17$), serum glucose ($p=0.23$), HbA1C ($p=0.98$), serum cholesterol ($p=0.82$), triglycerides ($p=0.68$), high-density lipoprotein C ($p=0.62$), low-density lipoprotein-C ($p=0.42$), GCS score ($p=0.53$), prior anticoagulant usage ($p=0.87$), prior antiplatelet usage ($p=0.76$), and ethnicity ($p=0.41$) (Table 1).

There was a significant difference in systolic blood pressure (SBP) and diastolic blood pressure (DBP) between the three groups ($p=0.04$ and $p=0.03$, respectively), with the intermediate volume expander group having the highest median SBP and DBP (Table 1). Similarly, there were significant differences in incidence of intraventricular hemorrhage between the three hematoma expansion groups ($p<.001$), as well as baseline hematoma ($p=0.0001$) and hematoma location ($p<.001$). In all three hematoma expansion groups, the hematoma location seemed to occur the highest at the basal ganglia, followed by cortical.

The fast volume expander group had the highest median (interquartile range) baseline NIHSS score 14.0 (7.0–20.0) compared to the slow volume expander 11.0 (5.0–18.0), $p=0.02$, and intermediate volume expander group 13.5 (6.0–20.0), $p=0.01$ (Figure 1). There was also a significant difference in the modified Rankin score (mRS) at 90 days between the three groups (Figure 2), with the fast volume expansion group having the highest proportion of a mRS score of 4–6 at 90 days (48.7% vs. 41.1% and 34.7% for the intermediate and slow volume expander group, respectively), $p=0.005$. The fast volume expander group also had the highest proportion of mortality at 90 days (17.9%) compared to the slow volume expander (9.1%) and intermediate volume expander (11.1%), $p=0.01$.

Multivariate analysis for risk factors associated with a higher mRS (3–6) at 90 days

Figure 3 illustrates a multiple binary logistic regression model to identify significant independent factors associated with the development of a higher mRS score at 90 days after selecting important and significant variables at bivariate analysis. Smoking, male sex, SBP and DBP were not independent predictors of a higher mRS at 90 days. Age (aOR 1.03, 95% CI: 1.02–1.04, $p<.001$), moderate stroke (aOR 3.21, 95% CI: 1.79–5.75, $p<.001$), severe stroke (aOR 27.0, 95% CI: 15.9–45.9, $p<.001$) and fast hematoma

expansion rate (aOR 1.77, 95% CI: 1.10–2.85, $p=0.02$) were identified as significant predictors of a poor outcome at 90 days. Site of bleed and intraventricular hemorrhage were also not identified as significant predictors of a higher mRS score at 90 days.

Multivariate analysis for risk factors associated with mortality at 90 days

Figure 4 illustrates a multiple binary logistic regression model to identify significant independent factors associated with mortality at 90 days after selecting important and significant variables at bivariate analysis. Age, smoking, male sex, SBP and DBP were not independent predictors of mortality at 90 days. Moderate stroke was not a significant predictor of mortality at 90 days (aOR 2.10, 95% CI: 0.72–6.15, $p=0.18$). However, severe stroke (defined as an NIHSS > 10) was a significant predictor of mortality at 90 days (aOR 11.4, 95% CI: 4.58–28.5, $p<.001$). Fast hematoma expansion rate was marginally associated with mortality at 90 days (aOR 1.79 95% CI: 0.99–3.20, $p=0.05$).

DISCUSSION

Hematoma expansion (HE) is an independent predictor of poor outcome and mortality. It has a modifiable nature, and hence a target for interventions in the management of ICH. The rate of expansion is highest in the earlier hours after onset and it decreases with time. Gaby Abou Karam et al. examined the association of HE with neurological deterioration (ND), functional outcome, and mortality among those with hyperacute HE versus those with HE in later hours after ICH onset, and showed that HE was higher among those scanned within the first 3 hours, compared to those scanned at 3–24 hours.¹¹ A recent individual patient-level meta-analysis showed that the majority of HE occurred early after ICH onset, the rate of decline in the probability of ICH growth was steepest during 0.5–3 h after symptom onset, and the predicted probability of ICH growth peaked at a volume of approximately 75 mL.¹² Four simple to collect predictors were identified to be associated with ICH growth: time from symptom onset to baseline imaging, initial ICH volume, antiplatelet (AP) use, and anti-coagulant (AC) use.¹²

While there is variability between studies regarding what defines ICH expansion, most studies have defined hematoma expansion using baseline CT, and 6- or 24-hour CT scans and

Table 1: Summary of group differences

	Slow Volume Expander (n=963)	Intermediate Volume Expander (n=180)	Fast Volume Expander (n=117)	p-value ^a
Age	49.0 (41.0–58.0)	49.0 (42.0–59.0)	50.0 (40.5–57.0)	0.61
Gender (male)	810 (84.1)	147 (81.7)	95 (81.2)	0.56
Smoking	110 (11.4)	17 (9.4)	7 (6.0)	0.17
Systolic BP, mm Hg	180.0 (154.0–206.0)	184.0 (160.0–211.8)	177.0 (146.5–197.0)	0.04
Diastolic BP, mm Hg	106.0 (90.0–123.0)	107.0 (94.0–129.0)	101.0 (87.5–116.0)	0.03
Serum glucose	7.4 (6.2–9.7)	7.4 (6.1–9.9)	8.1 (6.3–11.0)	0.23
Baseline hematoma volume	5.6 (2.8–9.8)	20.5 (17.2–26.8)	36.1 (28.8–48.1)	0.0001
Any IVH				<.001
<i>Yes</i>	262 (27.2)	83 (46.1)	68 (58.1)	
<i>No</i>	701 (72.8)	97 (53.9)	49 (41.9)	
Hematoma location				<.001
<i>Basal ganglia</i>	604 (62.7)	129 (71.7)	80 (68.4)	
<i>Thalamus</i>	176 (18.3)	4 (2.2)	1 (0.9)	
<i>White matter</i>	10 (1.0)	0 (0)	1 (0.9)	
<i>Cortical</i>	173 (18.0)	47 (26.1)	35 (29.9)	
Prior anticoagulant				0.87
<i>Yes</i>	25 (2.6)	6 (3.3)	3 (2.6)	
<i>No</i>	937 (97.4)	174 (96.7)	114 (97.4)	
Prior antiplatelet				0.76
<i>Yes</i>	108 (11.2)	18 (10.0)	15 (12.8)	
<i>No</i>	855 (88.8)	162 (90.0)	102 (87.2)	
Ethnicity				0.41
<i>Qatari</i>	193 (20.0)	40 (22.2)	35 (29.9)	
<i>Middle Eastern</i>	553 (57.4)	102 (56.7)	55 (47.0)	
<i>Far Eastern</i>	180 (18.7)	31 (17.2)	24 (20.5)	
<i>African</i>	28 (2.9)	6 (3.3)	2 (1.7)	
<i>Caucasian</i>	9 (0.9)	1 (0.6)	1 (0.9)	
HbA1C	5.8 (5.4–6.8)	6.0 (5.4–6.8)	5.9 (5.4–7.0)	0.98
Serum cholesterol	4.5 (3.9–5.3)	4.6 (3.7–5.4)	4.5 (3.6–5.3)	0.82
Triglycerides	1.3 (1.0–1.8)	1.4 (1.0–1.9)	1.2 (0.9–2.0)	0.68
HDL	1.0 (0.84–1.2)	1.0 (0.81–1.2)	1.0 (0.80–1.2)	0.62
LDL	2.8 (2.2–3.5)	2.7 (2.1–3.5)	2.8 (2.0–3.4)	0.42
GCS score	15.0 (12.0–15.0)	15.0 (11.0–15.0)	15.0 (10.0–15.0)	0.53
NIHSS	11.0 (5.0–18.0)	13.5(6.0–20.0)	14.0(7.0–20.0)	0.003
mRS at 90 days	3.0 (1.0–4.0)	3.0 (1.0–4.75)	3.0 (2.0–5.0)	0.002
Mortality at 90 days	88 (9.1)	20 (11.1)	21 (17.9)	0.01

Data are expressed as n(%), or median (interquartile interval) as appropriate.

^ap-values are based on Pearson χ^2 and Fisher's Exact test (for categorical variables) and Kruskal-Wallis test (with Dunn's post-hoc test performed)

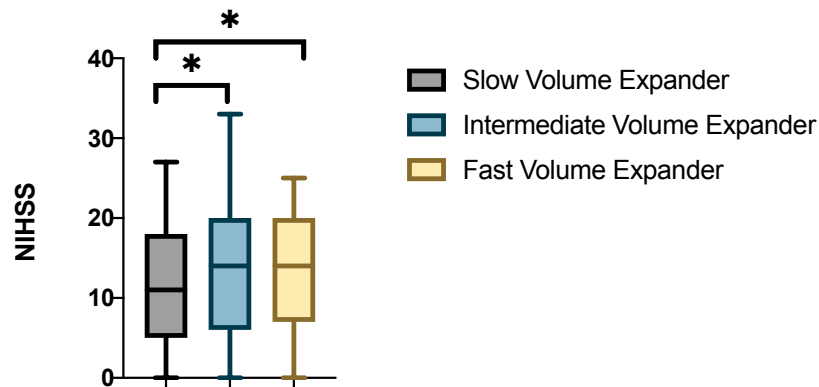


Figure 1. Median NIHSS score between the different hematoma expansion groups
* $p < 0.05$

looked at the absolute increase in ICH volume. We expressed the rate of expansion as the ratio between hematoma volume [mL] and time [h] from onset to arrival imaging acquisition and created risk categories for the rate of ICH expansion. We showed that compared to slow (<5 ml/hr) and intermediate (5–10 ml/hr) expanders, fast expanders (>10 ml/hr) had the highest mRS score at 90 days and the highest proportion of mortality at 90 days.

These findings hold value in the context of recent trials of anti-coagulation reversal, such as the ANNEXA trial, which showed that Andexanet Alfa can slow down the rate of ICH expansion and the rate of NIHSS increase in anti-coagulant associated ICH.¹³ Since ICH associated with the use of antithrombotic medications (antiplatelet agents or anticoagulants) have larger baseline hematoma volumes, more hematoma expansion and higher case fatality¹⁴, a feasibility study to assess the relative benefit of Andexanet Alpha in fast expanders might be fruitful, given that this group carries worse prognosis, as observed

in our study, and similar studies performed by Rodriguez-Luna *et al.*^{15,16}

Hemostatic therapy was attempted in the past in symptomatic ICH patients with early CT signs predictive of hematoma growth, such as the spot sign and black-hole sign. These high risk patients with imaging biomarkers of expansion were identified as candidates for hemostatic therapy in randomized-controlled trials (RCTs) such as STOP-IT¹⁷, SPOTLIGHT¹⁸, STOP-AUST¹⁹, TRAIGE²⁰, and TICH-2²¹, but none of them showed a statistically significant reduction in hematoma growth. All of these trials were conducted using imaging markers predictive of hematoma growth. Rate of ultra-early hematoma expansion similarly predicts outcomes post-ICH as seen in our current study and previous ultra-early hematoma growth studies.^{15,16} Hence, studying the efficacy of hemostatic therapy in ICH patients stratified by the rate of expansion holds promise, with most benefit expected in fast-expanders.

Calculating the rate of expansion only requires a CT head (CTH), and this can especially be

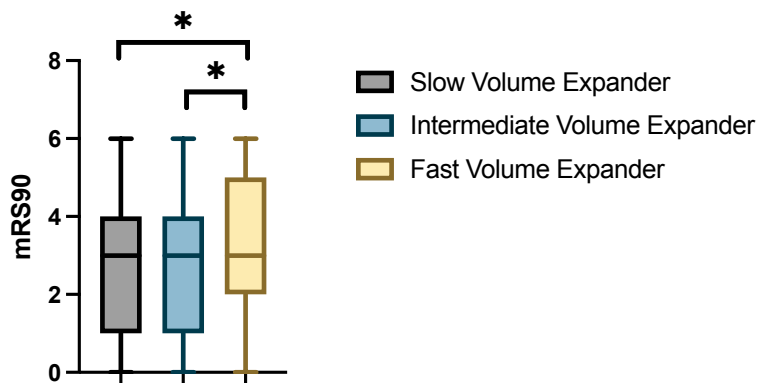


Figure 2. Median mRS score at 90 days between the different hematoma expansion groups
* $p < 0.05$

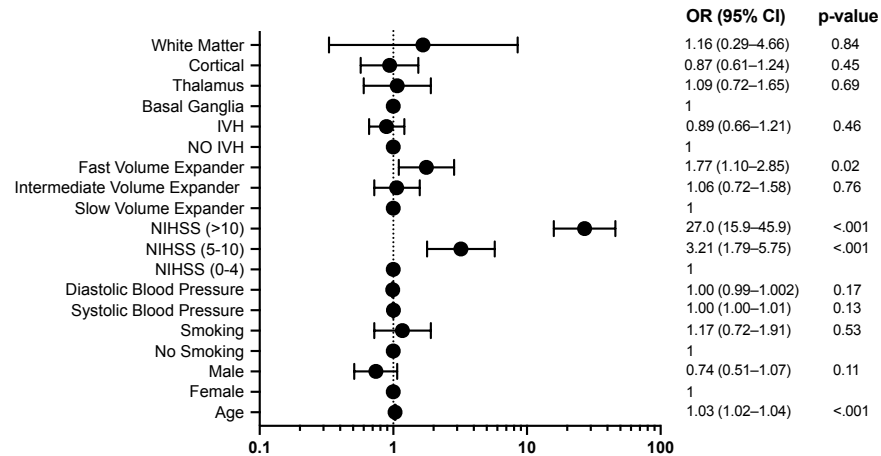


Figure 3. Multivariate logistic regression analysis of the risk factors associated with a high mRS score (4-6) at 90 days

helpful in resource constrained settings such as in low to middle income countries, and in patients with chronic kidney disease in whom contrast administration could be harmful. Also, since recruitment of patients with high-risk ICH is difficult into RCTs because of strict selection criteria and the difficulty of obtaining emergency computed tomography angiography (CTA) routinely, using just CTH and not CTAs could make recruitment into future RCTs easier.²²

Some limitations should be noted in the current study. Our patient sample is composed mainly of Middle eastern ethnicity (Qatari, Arabs), South Asian and Far Eastern (Asians), therefore, our results might have differed if we recruited patients of other ethnicities. Second, the time of onset was defined as the time of symptoms onset or the last time seen normal and depending on who was

around the patient or how accurately the patient could recall when their symptoms began, this could lead to inaccuracies in the time of onset reported.

In conclusion, rate of hematoma expansion is a useful predictor of functional outcomes in patients with acute supratentorial ICH in the Qatari population. Since its only pre-requisite is a CT head, it can easily be obtained even in resource limited settings.

DISCLOSURE

Ethics: The studies were approved by the Institutional Review Board of the Medical Research Centre at Hamad Medical Corporation (MRC-01-18-102).

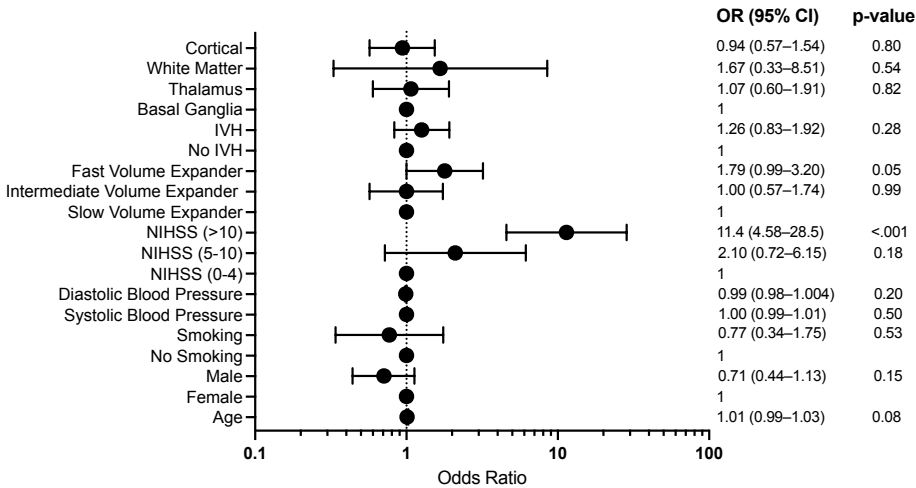


Figure 4. Multivariate logistic regression analysis of the risk factors associated with mortality at 90 days

Data availability: Data available upon reasonable request.

Financial support: None

Conflicts of interest: None

REFERENCES

1. Poon MTC, Fonville AF, Salman RAS. Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry* 2014;85(6):660-7. doi:10.1136/jnnp-2013-306476
2. Pinho J, Costa AS, Araújo JM, Amorim JM, Ferreira C. Intracerebral hemorrhage outcome: A comprehensive update. *J Neurol Sci* 2019;398:54-66. doi:10.1016/j.jns.2019.01.013
3. 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(2):167-76. doi:10.1016/S1474-4422(09)70340-0
4. Haupenthal D, Kuramatsu JB, Volbers B, et al. Disability-Adjusted life-years associated with intracerebral hemorrhage and secondary injury. *JAMA Netw Open* 2021;4(7):e2115859. doi:10.1001/jamanetworkopen.2021.15859
5. Dowlatshahi D, Demchuk AM, Flaherty ML, Ali M, Lyden PL, Smith EE. Defining hematoma expansion in intracerebral hemorrhage. *Neurology* 2011;76(14):1238-44. doi:10.1212/WNL.0b013e3182143317
6. Davis SM, Broderick J, Hennerici M, et al. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. *Neurology* 2006;66(8):1175-81. doi:10.1212/01.wnl.0000208408.98482.99
7. Haupenthal D, Schwab S, Kuramatsu JB. Hematoma expansion in intracerebral hemorrhage – the right target? *Neurol Res Pract* 2023;5(1):36. doi:10.1186/s42466-023-00256-6
8. Hemphill JC, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke* 2001;32(4):891-7. doi:10.1161/01.str.32.4.891
9. Broderick JP, Brott TG, Duldner JE, Tomsick T, Huster G. Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality. *Stroke* 1993;24(7):987-93. doi:10.1161/01.str.24.7.987
10. Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ* 1976;54(5):541-53.
11. Abou Karam G, Chen MC, Zeevi D, et al. Time-dependent changes in hematoma expansion rate after supratentorial intracerebral hemorrhage and its relationship with neurological deterioration and functional outcome. *Diagnostics* 2024;14(3):308. doi:10.3390/diagnostics14030308
12. Al-Shahi Salman R, Frantzas J, Lee RJ, et al. Absolute risk and predictors of the growth of acute spontaneous intracerebral haemorrhage: a systematic review and meta-analysis of individual patient data. *Lancet Neurol* 2018;17(10):885-94. doi:10.1016/S1474-4422(18)30253-9
13. Connolly SJ, Crowther M, Eikelboom JW, et al. Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. *N Eng J Med* 2019;380(14):1326-35. doi:10.1056/NEJMoa1814051
14. Seiffge DJ, Fandler-Höfler S, Du Y, et al. Intracerebral haemorrhage - mechanisms, diagnosis and prospects for treatment and prevention. *Nat Rev Neurol* 2024;20(12):708-23. doi:10.1038/s41582-024-01035-w
15. Rodriguez-Luna D, Coscojuela P, Rubiera M, et al. Ultraearly hematoma growth in active intracerebral hemorrhage. *Neurology* 2016;87(4):357-64. doi:10.1212/WNL.0000000000002897
16. Rodriguez-Luna D, Rubiera M, Ribo M, et al. Ultraearly hematoma growth predicts poor outcome after acute intracerebral hemorrhage. *Neurology* 2011;77(17):1599-604. doi:10.1212/WNL.0b013e3182343387
17. Flaherty M. The spot sign for predicting and treating intracerebral hemorrhage growth study. *clinicaltrials.gov*; 2018. Accessed February 15, 2025. <https://clinicaltrials.gov/study/NCT00810888>
18. Gladstone D. 'Spot Sign' Selection of Intracerebral Hemorrhage to Guide Hemostatic Therapy (SPOTLIGHT). *clinicaltrials.gov*; 2018. Accessed February 15, 2025. <https://clinicaltrials.gov/study/NCT01359202>
19. Meretoja A, Churilov L, Campbell BCV, et al. The spot sign and tranexamic acid on preventing ICH growth--Australasia Trial (STOP-AUST): protocol of a phase II randomized, placebo-controlled, double-blind, multicenter trial. *Int J Stroke* 2014;9(4):519-24. doi:10.1111/ijss.12132
20. Liu J, Nie X, Gu H, et al. Tranexamic acid for acute intracerebral haemorrhage growth based on imaging assessment (TRAIGE): a multicentre, randomised, placebo-controlled trial. *Stroke Vasc Neurol* 2021;6(2):160-9. doi:10.1136/svn-2021-000942
21. Sprigg N, Robson K, Bath P, et al. Intravenous tranexamic acid for hyperacute primary intracerebral hemorrhage: Protocol for a randomized, placebo-controlled trial. *Int J Stroke* 2016;11(6):683-94. doi:10.1177/1747493016641960
22. Nie X, Liu J, Liu D, et al. Haemostatic therapy in spontaneous intracerebral haemorrhage patients with high-risk of haematoma expansion by CT marker: a systematic review and meta-analysis of randomised trials. *Stroke Vasc Neurol* 2021;6(2):170-9. doi:10.1136/svn-2021-000941