Published in final edited form as:
Stroke. 2014 November ; 45(11): 3293–3297. doi:10.1161/STROKEAHA.114.005570.

Spot sign on 90 second delayed CTA improves sensitivity for hematoma expansion and mortality: a prospective study

Viesha A. Ciura, M.D.[1], **H. Bart Brouwers, M.D.**[2,3,4,5,6], **Raffaella Pizzolato, M.D.**[1], **Claudia J. Ortiz, M.D.**[1], **Jonathan Rosand, M.D., M.Sc.**[3,4,5,6], **Joshua Goldstein, M.D., Ph.D.**[4,5,6,7], **Steven M. Greenberg, M.D.**[5], **Stuart R Pomerantz, M.D.**[1], **R. Gilberto Gonzalez, M.D., Ph.D.**[1], and **Javier M. Romero, M.D.**[1]

[1] Division of Neuroradiology, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston [2] Department of Neurosurgery, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands [3] Center for Human Genetic Research, Massachusetts General Hospital, Harvard Medical School, Boston [4] Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston [5] Hemorrhagic Stroke Research Group, Massachusetts General Hospital, Harvard Medical School, Boston [6] J. Philip Kistler Stroke Research Center, Massachusetts General Hospital, Harvard Medical School, Boston [7] Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston

Abstract

Background and Purpose—The CTA spot sign is a validated biomarker for poor outcome and hematoma expansion in intracerebral hemorrhage (ICH). The spot sign has proven to be a dynamic entity, with multimodal imaging proving to be of additional value. We investigated whether the addition of a 90 second delayed CTA acquisition would capture additional ICH patients with the spot sign and increase the sensitivity of the spot sign.

Methods—We prospectively enrolled consecutive ICH patients undergoing first pass and 90 second delayed CTA over 18 months at a single academic center. Uni- and multivariate logistic regression were performed to assess clinical and neuroimaging covariates for relationship with hematoma expansion and mortality.

Results—Sensitivity of the spot sign for hematoma expansion on first pass CTA was 55%, which increased to 64% if the spot sign was present on either CTA acquisition. In multivariate analysis the spot sign presence was associated with significant hematoma expansion: odds ratio (OR) 17.7 (95% CI 3.7-84.2, p=0.0004), 8.3 (95% CI 2.0-33.4, p=0.004), and 12.0 (95% CI 2.9-50.5, p=0.0008) if present on first pass, delayed, or either CTA acquisition respectively. Spot sign presence on either acquisitions was also significant for mortality.

Correspondence Javier M. Romero, M.D. Division of Neuroradiology, Massachusetts General Hospital 55 Fruit Street, Gray 2, Rm 273A Boston, MA 02114 USA T: +1 (617) 724-7095 F: +1 (617) 724-3338 jmromero@mgh.harvard.edu.

Disclosures

V.A. Ciura, None ; **H.B. Brouwers**, Research grant NIH-NINDS; **R. Pizzolato**, None; **C.J. Ortiz**, None; **J. Rosand**, Research Grant NIH, Consultant Boehringer Ingelheim; **J.N. Goldstein**, Research Grant NIH-NINDS; **S.M Greenberg**, None; **S.R. Pomerantz**, Research fellow salary support GE Healthcare; **R.G. Gonzalez**, None; **J.M. Romero**, None.

Conclusions—We demonstrate improved sensitivity for predicting hematoma expansion and poor outcome by adding a 90 second delayed CTA, which may enhance selection of patients that may benefit from hemostatic therapy.

Keywords

Intracerebral Hemorrhage; Hematoma Expansion; CTA Spot Sign; Mortality; CT angiography

INTRODUCTION

Spontaneous intracerebral hemorrhage (ICH) accounts for 8-15% of all strokes, [1] and is the most fatal form of stroke, with a mortality rate of almost 50% within the first month, and 80% rate of dependency at six months from onset. [2] The incidence of spontaneous ICH has not changed in the last three decades, [3] and remains without a proven specific treatment.

Several factors have been implicated as predictors of morbidity and mortality, including baseline hematoma volume, Glasgow coma scale (GCS) score, presence of intraventricular hemorrhage (IVH), and age. [4-6] Independent of these factors, hematoma expansion has been described as a determinant of both mortality and functional outcome, [6,7] making attenuation of growth an attractive and potentially modifiable therapeutic target.

A trial of recombinant activated factor VII (rFVIIa) generated optimism by demonstrating reduction in hematoma expansion; however it failed to show improvement in clinical outcome, and raised questions about the safety of rFVIIa given the thromboembolic complications. [8] The discrepant results may have been due to inclusion of a large number of subjects that did not expand, and were therefore not likely to benefit from hemostatic therapy.

Recently, the computed tomography angiography (CTA) spot sign has been validated in several studies as an imaging biomarker for hematoma expansion and poor outcome. [9-15] CTA spot sign has various descriptions and the outcome variables and definitions of hematoma expansion are not constant across studies, [16] the results are consistent irrespective of definition, spot sign presence reliably predicts expansion. The largest prospective study, PREDICT, demonstrated sensitivity of 51% for hematoma expansion when the spot sign was present on routine arterial phase imaging. [15] Additional studies have shown that the spot sign is a dynamic entity, which is also present on delayed CTA, venous phase CTA, dynamic CTA, postcontrast CT, and CT perfusion (CTP). [12,17-23] We investigated whether the addition of a 90 second delayed CTA acquisition would capture additional ICH patients with the spot sign and increase the sensitivity for predicting hematoma expansion and poor outcome.

METHODS

Patients

The study protocol was approved by the Massachusetts General Hospital institutional ethics review board. Subjects were enrolled prospectively, from February 2012 to August 2013, at a single academic center. Consecutive patients with spontaneous ICH who underwent a non-

contrast CT (NCCT) followed by computed tomography angiography (CTA) with 90 second delayed acquisition at the time of presentation were included. Patients with secondary ICH, including trauma, an underlying neoplasm or vascular malformation, hemorrhagic venous infarct or hemorrhagic conversion of ischemic stroke were excluded from the study. Patients were not excluded based on time from symptom onset to CTA. Patients that underwent surgery for hematoma evacuation or died before a follow-up CT was performed were excluded from the primary analysis, but included in a secondary analysis assessing functional outcome.

Clinical Information

Baseline demographic and clinical variables are listed in Table 1.

Image Acquisition

All patients enrolled in this study underwent NCCT, immediately followed by CTA of the head or head and neck, with a 90 second delayed acquisition through the hematoma volume, using strict standard departmental protocols on a 16- or 64-section helical MDCT scanner. The first pass CTA acquisition was performed using a semiautomated attenuation triggering SmartPrep (GE Healthcare) technique, injecting 65 to 85 mL at 4 to 5 mL/s. For first pass CTA, the following parameters were applied: 120 kV, 235 mA, 0.5 s/rotation, table speed of 20.6 mm/rotation, and 0.625 mm section thickness. To mitigate radiation, the delayed CTA acquisition included only the hematoma volume of interest and mAs was reduced by almost half (125 mA, 0.5 s/rotation). A follow-up NCCT of the head was performed within 24 hours of the CTA examination.

Image Analysis

All CTA studies were independently reviewed by two board-certified radiologists (with two years and 11 years of dedicated neuroradiology experience (VC and JR), with differences in reader interpretation adjudicated by consensus agreement. CTA source images were to determine the presence of the spot sign. The spot sign was defined using the following criteria: (1) ≥ one focus of contrast pooling within the ICH; (2) with an attenuation ≥120 HU; (3) discontinuous from normal or abnormal vasculature adjacent to the ICH; and (4) of any size and morphology. [12] The presence of the spot sign and spot sign characteristics were recorded, as well as presence of IVH.

Baseline and follow-up NCCT ICH volumes were calculated independently, using Analyze 10.0 (Mayo Clinic, Rochester, Minnesota) software. IVH volume was not included in the volume analysis. Significant hematoma expansion was defined as an absolute increase greater than 6 mL or an increase of greater than 33% from baseline ICH volume. [15,24]

Statistical Analysis

We performed a prospective analysis of retrospectively collected data. Discrete variables are summarized as count [percentage (%)] and continuous variables as mean [standard deviation (SD)] or median (interquartile range) when appropriate. We assessed the spot sign and its potential association with hematoma expansion (dichotomous outcome), starting with univariate logistic regression. Predictors significant at the $p < 0.20$ level in univariate

analysis, in addition to age and sex, were subsequently tested for an independent association with the outcome of interest in a multivariable logistic regression model. No interaction terms were included, since these are not well known in the appearance of spot sign. Subsequently, we calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy, using standard methods, to determine the accuracy of the spot sign in predicting hematoma expansion on first pass, delayed, or either CTA acquisition, separately. The threshold of significance was set at $p < 0.05$. All statistical analyses were performed using JMP Pro version 9.0 (SAS Institute Inc, Cary, NC).

RESULTS

Although a total of 121 patients met the inclusion criteria, only 74 (61%) had a follow-up NCCT within 24 hours and therefore met the primary outcome criteria for assessing hematoma expansion. For the secondary analysis, assessing in-hospital mortality, all 121 patients were included. In addition, functional status at discharge was available for 117 (97%) of patients (the remaining four subjects had incomplete medical records/discharge summaries). Of the 47 patients excluded from the primary analysis, 25 died before follow-up, 9 underwent surgery, 7 had a follow-up MRI rather than CT, and 6 had no follow-up for unknown reasons. These excluded patients had a high spot sign positive rate of 45%, and 90% died in hospital.

Inter-reader reliability for detection of the spot sign was excellent (kappa of 0.96), which is similar or better than previously published studies which report a kappa ranging from 0.77 to 0.94. [9,10,12,14]

Delayed spot sign correlation with hematoma expansion

All baseline characteristics are summarized in tables 1 and 2. In summary, of the 74 patients included in the primary analysis, 15 had a spot sign present on first pass, delayed, or both CTA acquisitions. The rate of hematoma expansion overall was 15%, with 47% expansion in the spot sign positive group and 7% expansion in the spot sign negative group. The median baseline hematoma volume was 19.1 mL (IQR 5.0-40.9) in the spot sign negative group and 54.6 (IQR 28.5-86.5) in the spot sign positive group.

Accuracy measures for the spot sign on first pass CTA were: sensitivity 55%, specificity 94%, PPV 60%, NPV 92%, and accuracy 88%. Accuracy measures for the spot sign on delayed CTA were: sensitivity 55%, specificity 87%, PPV 43%, NPV 92%, accuracy 82%. Accuracy measures for the spot sign on either CTA acquisition were: sensitivity: 64%, specificity 87%, PPV 47%, NPV 93%, accuracy 84%. These values are summarized in Table 3.

In the univariate analysis, warfarin, time to scan, initial volume and spot sign presence was associated with significant hematoma expansion. In multivariate analysis adjusted for age, sex, warfarin use, time to CTA, and baseline hematoma volume, the spot sign on both CTA acquisition and warfarin remained associated with hematoma expansion. (Table 4)

Delayed spot sign correlation with mortality and functional status

The secondary analysis included 121 patients, 36 of which had a spot sign present on first pass, delayed, or both CTA acquisitions. The spot sign was present on first pass CTA only in one patient, both acquisitions in 20 patients, and on the delayed 90 second acquisition only in 15 patients.

In univariate analysis, glucose, hypertension, spot sign presence, and warfarin were associated with mortality. Multivariable analysis determined that the spot sign on either CTA acquisition (p= <0.0001) and glucose (p=0.04) were independent predictors of mortality (Table 4).

Modified Rankin scale (mRS) at discharge ranged from 1 to 6 in all groups. The median mRS in the spot sign negative groups was 4, with 79.5% of patients having a poor outcome (mRS≥3). The median mRS in the groups of patients with a spot sign on first pass CTA, delayed CTA or either CTA acquisition was 6, with poor outcome in 95.2, 97.0 and 97.1% of patients in those respective groups. We detected that of the 9 patients who underwent surgery, 6 survived and 3 died, of the survivors 1 had good clinical outcome and 5 poor clinical outcome.

DISCUSSION

The addition of a delayed CTA acquisition captures additional patients destined to undergo significant hematoma expansion and increases the predictive ability of the spot sign. We observed a sensitivity of 55% for predicting hematoma expansion if the spot sign was present on first pass CTA, which increased to 64% if the spot sign was present on either CTA acquisition. Previous studies of the spot sign in predicting hematoma expansion have reported sensitivities ranging from 51 to 100% [9,10,12-15,18,25,26], however many of these studies were limited by a small number of patients, their retrospective nature, and heterogeneity in definitions of the spot sign and hematoma expansion. PREDICT was the largest prospective study, reporting sensitivity of 51%, however it was a multicenter trial with CTA protocol varying by institution. [15] The authors of PREDICT recently performed a post-hoc analysis on their data and found that >20% of their CTAs were acquired in the venous phase, and that later image acquisition improved the frequency of spot sign detection. [23]

The spot sign is a dynamic entity, when present on the first pass CTA acquisition usually persists on the delayed acquisition (in all but one patient), and that almost half of spot sign positive patients (15/36) only demonstrated the sign on the delayed CTA acquisition.

Previous retrospective studies have examined the utility of contrast extravasation or leakage on post-contrast CT (PCCT). Hallevi *et al.* [18] demonstrated that contrast extravasation on PCCT was a more sensitive predictor of hematoma expansion than the spot sign, and Ederies *et al.* [13] demonstrated that PCCT leakage in addition to the spot sign improved sensitivity for hematoma expansion. More recent studies using dynamic CTA [17] and CTP [20,21] showed improved detection of the spot sign and increased accuracy for predicting outcome and hematoma expansion. Although it is clear that the spot sign is a dynamic finding, there is no

accepted consensus regarding the timing of image acquisition. In our experience the 90 second delayed CTA acquisition produces optimal and reproducible results. Some of the uncertainty regarding optimal timing for capturing the CTA spot sign has to do with the biological underpinnings of the finding, which is not well understood. In patients with underlying vascular disease such as hypertensive lipohyalinosis, the primary source of hemorrhage is likely from rupture of a diseased vessel, which triggers a cascade of secondary bleeding as a result of mass effect which stretches and disrupts surrounding arteries as proposed by Fisher. [27]

Our prospective design included patients with large baseline hematoma volumes and late or unknown time to presentation and different follow up imaging, which differs from prior studies, in order to not exclude late expanders. PREDICT excluded patients with baseline ICH volume >100 mL and time from symptom onset >6 hours, which may have included patients destined to undergo hematoma expansion and may partly explain its modest reported sensitivity. Our results are concordant with other studies which have shown that patients with the spot sign have larger hematoma volumes at presentation and present earlier, [15,28] and that warfarin is an independent predictor of hematoma expansion. [4,19] Glucose, as in prior reports was a predictor of mortality. [29]

Goldstein *et al.* demonstrated that contrast extravasation on CTA was a significant predictor of hematoma expansion independent of time to presentation, [10] and Brouwers *et al.* showed that the CTA spot sign accurately predicts hematoma expansion even in patients with a delayed presentation (beyond 6 hours) or unknown symptom onset. [30] Given that there is no proven treatment of benefit for ICH, more inclusive patient selection criteria may be key in designing future trials of hemostatic therapy.

Limitations of our study include that it was performed at a single center with a selected population, with a high rate of in-hospital mortality and therefore lack of follow up imaging on a large number of patients. Patients without follow–up imaging also had a high proportion of spot sign, which may have underestimated the predictive value of the spot sign for ICH expansion. There was no standardized timing for the follow up NCCT, which ranged from 0.9 to 23.9 hours. The additional 90 second delayed CTA acquisition leads to increased radiation to the patient, however, we modified our protocol to keep radiation dose as low as possible.

The spot sign has proven itself as an attractive selection tool for therapeutic interventions in patients with ICH, in an attempt to halt or decrease hematoma expansion. There are several trials ongoing, including STOP-IT (the spot sign for predicting and treating ICH growth study) and SPOTLIGHT (spot sign selection of intracerebral hemorrhage to guide hemostatic therapy), comparing recombinant factor VIIa (rFVIIa) to placebo in spot sign positive patients. An ancillary study of ATACH-II (antihypertensive treatment of acute cerebral hemorrhage) seeks to determine whether patients with the spot sign will benefit from intensive blood pressure reduction. [31]

CONCLUSION

The discovery of imaging biomarkers such as the spot sign is an ever expanding field of study with encouraging results. We demonstrate improved sensitivity for predicting hematoma expansion and poor outcome by adding the 90 second delayed acquisition to our standard CTA protocol, which may enhance selection of patients that may benefit from hemostatic therapy.

Acknowledgments

None

Sources of Funding

Dr. Brouwers was supported by the NIH-NINDS SPOTRIAS fellowship grant P50NS051343.

REFERENCES

1. Sudlow CL, Warlow CP. Comparable studies of the incidence of stroke and its pathological types: results from an international collaboration. International Stroke Incidence Collaboration. Stroke. 1997; 28:491–499. [PubMed: 9056601]
2. Flaherty ML, Haverbusch M, Sekar P, Kissela B, Kleindorfer D, Moomaw CJ, et al. Long-term mortality after intracerebral hemorrhage. Neurology. 2006; 66:1182–1186. [PubMed: 16636234]
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; 9:167–176. [PubMed: 20056489]
4. 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; 24:987–993. [PubMed: 8322400]
5. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. Stroke. 2001; 32:891–897. [PubMed: 11283388]
6. Davis SM, Broderick J, Hennerici M, Brun NC, Diringer MN, Mayer SA, et al. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. Neurology. 2006; 66:1175–1181. [PubMed: 16636233]
7. Dowlatshahi D, Demchuk AM, Flaherty ML, Ali M, Lyden PL, Smith EE, et al. Defining hematoma expansion in intracerebral hemorrhage: relationship with patient outcomes. Neurology. 2011; 76:1238–1244. [PubMed: 21346218]
8. Mayer SA, Brun NC, Begtrup K, Broderick J, Davis S, Diringer MN, et al. Efficacy and safety of recombinant activated factor VII for acute intracerebral hemorrhage. N Engl J Med. 2008; 358:2127–2137. [PubMed: 18480205]
9. Wada R, Aviv RI, Fox AJ, Sahlas DJ, Gladstone DJ, Tomlinson G, et al. CT angiography “spot sign” predicts hematoma expansion in acute intracerebral hemorrhage. Stroke. 2007; 38:1257–1262. [PubMed: 17322083]
10. Goldstein JN, Fazen LE, Snider R, Schwab K, Greenberg SM, Smith EE, et al. Contrast extravasation on CT angiography predicts hematoma expansion in intracerebral hemorrhage. Neurology. 2007; 68:889–894. [PubMed: 17372123]
11. Kim J, Smith A, Hemphill JC 3rd, Smith WS, Lu Y, Dillon WP, et al. Contrast extravasation on CT predicts mortality in primary intracerebral hemorrhage. AJNR Am J Neuroradiol. 2008; 29:520–525. [PubMed: 18065505]
12. Delgado Almandoz JE, Yoo AJ, Stone MJ, Schaefer PW, Goldstein JN, Rosand J, et al. Systematic characterization of the computed tomography angiography spot sign in primary intracerebral hemorrhage identifies patients at highest risk for hematoma expansion: the spot sign score. Stroke. 2009; 40:2994–3000. [PubMed: 19574553]

13. Ederies A, Demchuk A, Chia T, Gladstone DJ, Dowlatshahi D, Bendavit G, et al. Postcontrast CT extravasation is associated with hematoma expansion in CTA spot negative patients. Stroke. 2009; 40:1672–1676. [PubMed: 19286577]
14. Li N, Wang Y, Wang W, Ma L, Xue J, Weissenborn K, et al. Contrast extravasation on computed tomography angiography predicts clinical outcome in primary intracerebral hemorrhage: a prospective study of 139 cases. Stroke. 2011; 42:3441–3446. [PubMed: 21980207]
15. Demchuk AM, Dowlatshahi D, Rodriguez-Luna D, Molina CA, Blas YS, Dzialowski I, et al. Prediction of haematoma growth and outcome in patients with intracerebral haemorrhage using the CT-angiography spot sign (PREDICT): a prospective observational study. Lancet Neurol. 2012; 11:307–314. [PubMed: 22405630]
16. Brouwers HB, Goldstein JN, Romero JM, Rosand J. Clinical applications of the computed tomography angiography spot sign in acute intracerebral hemorrhage: a review. Stroke. 2012; 43:3427–3432. [PubMed: 23132779]
17. Chakraborty S, Blacquiere D, Lum C, Stotts G. Dynamic nature of the CT angiographic “spot sign”. Br J Radiol. 2010; 83:e216–e219. [PubMed: 20846980]
18. Hallevi H, Abraham AT, Barreto AD, Grotta JC, Savitz SI. The spot sign in intracerebral hemorrhage: the importance of looking for contrast extravasation. Cerebrovasc Dis. 2010; 29:217–220. [PubMed: 20029193]
19. Delgado Almandoz JE, Yoo AJ, Stone MJ, Schaefer PW, Oleinik A, Brouwers HB, et al. The spot sign score in primary intracerebral hemorrhage identifies patients at highest risk of inhospital mortality and poor outcome among survivors. Stroke. 2010; 41:54–60. [PubMed: 19910545]
20. Koculym A, Huynh TJ, Jakubovic R, Zhang L, Aviv RI. CT perfusion spot sign improves sensitivity for prediction of outcome compared with CTA and postcontrast CT. AJNR Am J Neuroradiol. 2013; 34:965–970. [PubMed: 23124643]
21. Sun SJ, Gao PY, Sui BB, Hou XY, Lin Y, Xue J, et al. “Dynamic spot sign” on CT perfusion source images predicts haematoma expansion in acute intracerebral haemorrhage. Eur Radiol. 2013; 23:1846–1854. [PubMed: 23508276]
22. Dowlatshahi D, Wasserman JK, Momoli F, Petrcich W, Stotts G, Hogan M, et al. Evolution of computed tomography angiography spot sign is consistent with a site of active hemorrhage in acute intracerebral hemorrhage. Stroke. 2014; 45:277–280.
23. Rodriguez-Luna D, Dowlatshahi D, Aviv RI, Molina CA, Silva Y, Dzialowski I, et al. Venous phase of computed tomography angiography increases spot sign detection, but intracerebral hemorrhage expansion is greater in spot signs detected in arterial phase. Stroke. 2014; 45:734–739. [PubMed: 24481974]
24. Brott T, Broderick J, Kothari R, Barsan W, Tomsick T, Sauerbeck L, et al. Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke. 1997; 28:1–5. [PubMed: 8996478]
25. Murai Y, Takagi R, Ikeda Y, Yamamoto Y, Teramoto A. Three-dimensional computerized tomography angiography in patients with hyperacute intracerebral hemorrhage. J Neurosurg. 1999; 91:424–431. [PubMed: 10470817]
26. Wang YH, Fan JY, Luo GD, Lin T, Xie DX, Ji FY, et al. Hematoma volume affects the accuracy of computed tomographic angiography ‘spot sign’ in predicting hematoma expansion after acute intracerebral hemorrhage. Eur Neurol. 2011; 65:150–155. [PubMed: 21372573]
27. Fisher CM. Pathological observations in hypertensive cerebral hemorrhage. J Neuropathol Exp Neurol. 1971; 30:536–550. [PubMed: 4105427]
28. Becker KJ, Baxter AB, Bybee HM, Tirschwell DL, Abouelsaad T, Cohen WA. Extravasation of radiographic contrast is an independent predictor of death in primary intracerebral hemorrhage. Stroke. 1999; 30:2025–2032. [PubMed: 10512902]
29. Qureshi AI, Palesch YY, Martin R, Novitzke J, Cruz-Flores S, Ehtisham A, et al. Association of serum glucose concentrations during acute hospitalization with hematoma expansion, perihematomal edema, and three month outcome among patients with intracerebral hemorrhage. Neurocrit Care. 2011; 15:428–35. [PubMed: 21573860]
30. Brouwers HB, Falcone GJ, McNamara KA, Ayres AM, Oleinik A, Schwab K, et al. CTA spot sign predicts hematoma expansion in patients with delayed presentation after intracerebral hemorrhage. Neurocrit Care. 2012; 17:421–428. [PubMed: 22878870]

31. Goldstein J, Brouwers H, Romero J, McNamara K, Schwab K, Greenberg S, et al. SCORE-IT: the Spot Sign score in restricting ICH growth horizontal line an Atach-II ancillary study. J Vasc Interv Neurol. 2012; 5:20–25. [PubMed: 23230461]

Table 1

Baseline characteristics

Baseline characteristic	Spot sign positive (n=36)	Spot sign negative (n=85)	Univariate *p*-value
Age, mean (SD)	74 +/−16)	69(+/−15)	0.12
Sex (male), n (%)	22(61%)	45(53%)	0.43
Warfarin, n (%)	6(17%)	10(12%)	0.56
Hypertension, n (%)	29(81%)	63(75%)	0.64
Admit glucose (mg/dL), median (IQR)	156.5(128.5-185)	131(112.5-165.5)	0.048
Time from symptom onset to CTA (hrs), median (IQR)	2.8(1.2-5.3)	5.6(3.1-11.0)	0.0036
Baseline hematoma volume (mL), median (IQR)	81.1(37.1-123.0)	19.7(5.3-45.4)	<0.0001
Presence of IVH, n (%)	26(72%)	30(35%)	0.0003

SD = Standard Deviation; mg/dL = milligram/deciliter; IQR = Interquartile Range; hrs = hours; mL = milliliter; IVH = Intraventricular Hemorrhage

Table 2

Radiographic and clinical outcomes

Variable	All	No SS	SS on first pass CTA	SS on delayed CTA	SS on either CTA acquisition
Primary outcome – hematoma expansion					
Number of subjects (%)	74(100.0)	59(79.7)	10(13.5)	14(18.9)	15(20.3)
Baseline ICH volume (median, IQR)	24.3(5.8-53.5)	19.1(5.0-40.9)	32.9(22.3-64.7)	62.5(27.4-88.6)	54.6(28.5-86.5)
Follow-up ICH volume (median, IQR)	23.1(5.7-55.9)	20.2(5.2-39.5)	54.7(27.1-113.7)	79.3(27.1-112.8)	75.6(30.7-108.4)
Intraventricular extension	31(41.9)	23(39.0)	5(50.0)	7(50.0)	8(53.3)
Time to follow-up CT in hours (median, IQR)	6.4(4.8-10.5)	6.4(4.9-11.5)	4.7(4.0-7.2)	6.0(4.1-8.0)	6.3(4.1-8.7)
Hematoma expansion >6 mL or 33%	11(14.9)	4(6.8)	6(60.0)	6(42.9)	7(46.7)
Absolute change in volume in mL (median, IQR)	0.05(−1.8 to 1.4)	−0.1(−1.8 to 0.7)	12.1(1.0 to 30.2)	2.9(−3.4 to 20.0)	4.2(−3.4 to 20.3)
Absolute change in volume in % (median, IQR)	0.8(−8.2 to 7.7)	−2.2(−9.2 to 5.0)	49.4(2.8 to 82.6)	5.1(−4.1 to 74.2)	5.8(−4.1 to 71.4)
Secondary outcome – in-hospital mortality					
Number of subjects	121(100.0)	85(70.2)	21(17.4)	35(28.9)	36(29.8)
In-hospital mortality	48(39.7)	22(25.9)	15(71.4)	26(74.3)	26(72.2)
Secondary outcome – poor outcome at discharge					
Number of subjects	117(100.0)	83(70.9)	21(17.9)	33(28.2)	34(29.1)
mRS at discharge (median, range)	4(1-6)	4(1-6)	6(1-6)	6(1-6)	6(1-6)
Poor outcome (mRS≥3)	99(84.6)	66(79.5)	20(95.2)	32(97.0)	33(97.1)

SS = Spot Sign; CTA = Computed Tomography Angiography; ICH = Intracerebral Hemorrhage; IQR = Interquartile Range; mL = milliliter; mRS = Modified Rankin Scale

Table 3

Performance of the spot sign for predicting mortality and hematoma expansion

	Sensitivity	Specificity	PPV	NPV	Accuracy	OR (95% CI, *p*-value)
Primary outcome – hematoma expansion (>6 mL or 33%)						
SS on first pass CTA	0.55	0.94	0.60	0.92	0.88	17.7(3.7-84.2, 0.0004)
SS on delayed CTA	0.55	0.87	0.43	0.92	0.82	8.3(2.0-33.4, 0.004)
SS on either CTA acquisition	0.64	0.87	0.47	0.93	0.84	12.0(2.9-50.5 0.0008)
Secondary outcome – discharge mortality						
SS on first pass CTA	0.31	0.92	0.71	0.67	0.68	5.24 (1.5 to 17.3, 0.003)
SS on delayed CTA	0.54	0.88	0.74	0.74	0.74	8.4 (3.4-20.7, <0.0001)
SS on either CTA acquisition	0.54	0.86	0.72	0.74	0.74	8.5 (3.0 to 23.7, <0.0001)

SS = Spot Sign; CTA = Computed Tomography Angiography; PPV = Positive Predictive Value; NPV = Negative Predictive Value; OR = Odds Ratio; CI = Confidence Interval

Table 4

Multiple logistic regression analysis

Variable	Coefficient	Std.Error	P	Odds ratio	95% CI
Primary Outcome - Expansion					
Age	−0.01	0.03	0.68	0.98	0.92 to 1.05
Sex	−1.35	0.85	0.11	0.07	0.001 to 1.30
Warfarin	1.93	0.97	0.04	47.74	1.81 to 6617.98
Time to scan	−0.14	0.10	0.16	0.86	0.67 to 1.05
Initial volume	0.01	0.01	0.32	1.01	0.98 to 1.06
SS on either CTA acquisition	3.08	1.21	0.0008	12.0	2.90-50.50
Secondary Outcome - Mortality					
Age	0.02	0.01	0.11	1.03	0.99 to 1.06
Glucose	0.009	0.004	0.04	1.01	1 to 1.01
HTN	−1.19	0.64	0.06	0.30	0.08 to 1.07
Sex	−0.06	0.48	0.89	0.94	0.36 to 2.40
SS on First or Delayed	2.14	0.52	<0,0001	8.56	3.08 to 23.76
Surgery	−0.08	0.84	0.92	0.92	0.17 to 4.86
Warfarin	0.48	0.65	0.46	1.62	0.44 to 5.86

P = p-value; OR = Odds Ratio; CI = Confidence Interval; SS = Spot Sign; HTN = Hypertension.