Observational Study

Medicine

OPEN

The comprehensive comparison of imaging sign from CT angiography and noncontrast CT for predicting intracranial hemorrhage expansion

A comparative study

Gyung Ho Chung, MD, PhD[a], Ja Hong Goo, MD[b], Hyo Sung Kwak, MD, PhD[a,*], Seung Bae Hwang, MD, PhD[a]

Abstract

Expansion of intracranial hemorrhage (ICH) is an important predictor of poor clinical outcomes. Various imaging markers on non-contrast computed tomography (NCCT) or computed tomographic angiography (CTA) have been reported as predictors of ICH expansion. We aimed to compare the associations between various CT imaging markers and ICH expansion. Patients with spontaneous ICH who underwent initial NCCT, CTA, and subsequent NCCT between January 2016 and December 2019 were retrospectively identified. ICH expansion was defined as a volume increase of > 33% or > 6 mL. We analyzed the presence of imaging markers such as the black hole sign, blend sign, island sign, or swirl sign on initial NCCT or spot sign on CTA. An alternative free-response receiver operating characteristic curve analysis was performed using a 4-point scoring system based on the consensus of the reviewers. The predictive value of each marker was assessed using univariate and multivariate logistic regression analyses. A total of 250 patients, including 60 (24.0%) with ICH expansion, qualified for the analysis. Among the patients with spontaneous ICH, 118 (47.2%) presented with a black hole sign, 52 (20.8%) with a blend sign, 93 (37.2%) with an island sign, 79 (31.6%) with a swirl sign, and 56 (22.4%) with a spot sign. In univariate logistic regression, the initial ICH volume ($P = .038$), initial intraventricular hemorrhage (IVH) presence ($P < .001$), swirl sign ($P < .001$), and spot sign ($P < .001$) were associated with ICH expansion. Multivariate analysis confirmed that the presence of initial IVH (odds ratio, 4.111; $P = .002$) and spot sign (odds ratio, 109.5; $P < .001$) were independent predictors of ICH expansion. Initial ICH volume, IVH, swirl sign, and spot sign are associated with ICH expansion. The presence of spot signs and IVH were independent predictors of ICH expansion.

Abbreviations: BHS = black hole sign, BS = blend sign, CTA = computed tomographic angiography, ICH = intracranial hemorrhage, IS = island sign, IVH = intraventricular hemorrhage, NCCT = noncontrast computed tomography, ROC = receiver operating characteristic curve, SS = swirl sign.

Key words: CT angiography, hematoma expansion, intracranial hemorrhage, noncontrast computed tomography

1. Introduction

Early hematoma expansion occurs in approximately one-third of the patients with spontaneous intracerebral hemorrhage (ICH).[1] Hematoma expansion is highly predictive of neurological deterioration and is an independent predictor of mortality and functional outcome.[2–4] Therefore, predicting ICH expansion can be a crucial part of targeting patients for anti-expansion treatment.

Recently, various imaging markers on noncontrast computed tomography (NCCT) have been reported as predictors of ICH expansion, including the black hole sign (BHS), island sign (IS), swirl sign (SS), and blend signs (BS).[5–11] NCCT imaging markers are more readily available in clinical routine than CT angiography (CTA). In addition, contrast application may be associated with risks of allergic reactions to the contrast medium and renal dysfunction in some patients. However, several articles have

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Education (NRF-2020R1A2C1008089).

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

[a] Department of Radiology and Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeollabuk-do, Korea, [b] Department of Internal Medicine, Kangbuk Samsung Hospital, Jeollabuk-do, Korea.

**Correspondence: Hyo Sung Kwak, Radiology and Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, 567 Baekje-daero, deokjin-gu, Jeonju-si, Jeollabuk-do, 561-756, Republic of Korea (e-mail: kwak8140@jbnu.ac.kr).*

How to cite this article: Chung GH, Goo JH, Kwak HS, Hwang SB. The comprehensive comparison of imaging sign from CT angiography and noncontrast CT for predicting intracranial hemorrhage expansion: A comparative study. Medicine 2022;101:49(e31914).

Received: 9 August 2020 / Received in final form: 8 August 2022 / Accepted: 9 August 2022

http://dx.doi.org/10.1097/MD.0000000000031914

proposed the spot sign on CTA as a potential predictor of hematoma expansion. [10-14]

In this study, we aimed to clarify the association between 4 NCCT markers (BHS, IS, SS, and BS) or CTA spot sign and ICH expansion using univariate and multivariate logistic regression models.

2. Methods

The study protocol was approved by the Jeonbuk National University Hospital Institutional Review Board (JNU 2018-10-015-01) in South Korea. The requirement for informed consent was waived by our institutional review board from the relatives of the deceased.

2.1. Patients

This case-control study was a retrospective analysis of the institutional data of all patients who were admitted for treatment of ICH between January 2015 and December 2019. During this period, 365 patients were admitted for ICH treatment. The inclusion criteria of this study were as follows: age ≥ 18 years, history of spontaneous ICH, immediate NCCT within 1 hour after symptom onset, CTA examination within 1 hour after NCCT, and follow-up NCCT examination between 2 and 6 hours after CTA. The exclusion criteria for this study were as follows: brainstem or cerebellar hemorrhage; trauma-related hemorrhage; secondary ICH, such as ischemic transformation, tumor, vasculitis, Moyamoya disease, and venous infarction; previous lobar infarction history; and previous brain surgery history. Of 325 patients, 250 with spontaneous ICH and complete NCCT and CTA examination following our study protocol were enrolled in this study.

2.2. CT acquisition

Initial NCCT (Definition Flash; Siemens, Erlangen, Germany) with a slice thickness of 1.0 mm was obtained for all patients. Patients in our sample underwent NCCT, followed by CTA if it was detected, which was performed by scanning from the cerebral vertex to the aortic arch with 0.6-mm section thickness slices. Nonionic contrast media (80–120 milliliters; Xenetix, Guerbet, Aulnay-sous-Bois, France) was administered into the antecubital vein at 3 to 5 milliliters/second, and CTA source images for the evaluation of atherosclerosis or vascular malformation were post-processed and reformatted to create coronal, sagittal, and axial multiplanar images. Follow-up NCCT with a slice thickness of 1.0 mm was performed, except for patients who needed emergency operation.

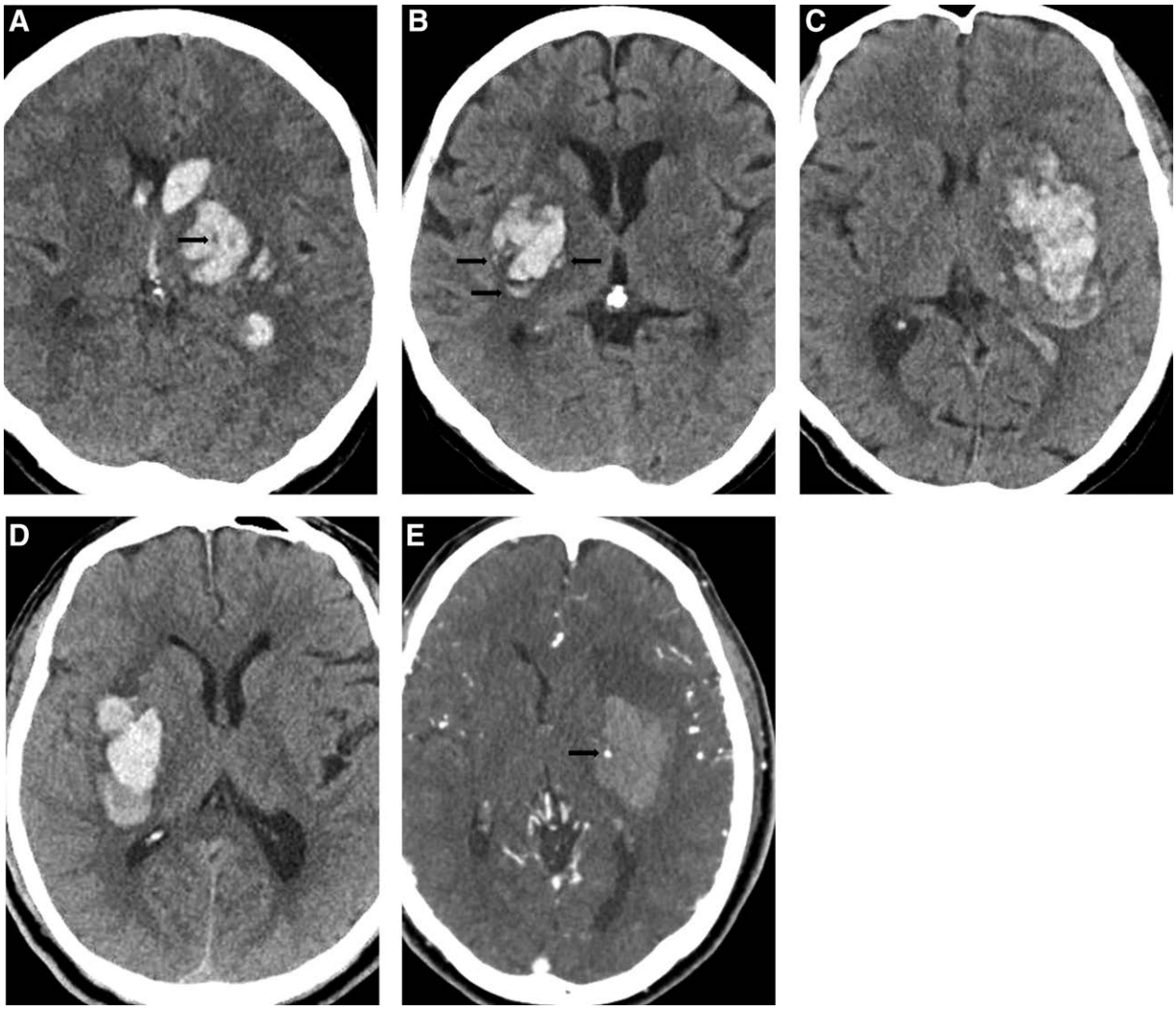

Figure 1. (A) Black hole sign. (B) Blend sign. (C) Island sign. (D) Swirl sign. (E) Spot sign.

Table 1

The demographic characteristics of patients with and without ICH expansion.

	Total (n = 250)	ICH expansion (n = 60)	No expansion (n = 190)	*P*
Age	65.8 ± 0.9	63.9 ± 1.8	65.8 ± 1.0	.344
Male, n (%)	130 (52.0)	30 (50.0)	100 (52.6)	.722
Hypertension, n (%)	150 (60.0)	33 (55.0)	117 (61.6)	.364
Diabetes, n (%)	60 (24.0)	14 (23.3)	46 (24.2)	.890
Smoking, n (%)	26 (10.4)	5 (8.3)	21 (11.1)	.547
Alcohol, n (%)	49 (19.6)	13 (21.7)	36 (18.9)	.644
Chronic renal disease, n (%)	11 (4.4)	4 (6.7)	7 (3.7)	.302
Liver disease, n (%)	15 (6.0)	5 (8.3)	10 (5.3)	.363
Cardiac disease, n (%)	7 (2.8)	0 (0.0)	7 (3.7)	.202
Systolic blood pressure	167.3 ± 2.3	164.6 ± 5.1	168.2 ± 2.5	.498
PT	12.5 ± 0.6	14.7 ± 2.0	11.9 ± 0.3	.695
aPTT	29.1 ± 0.4	29.5 ± 1.1	29.0 ± 0.5	.645
INR	1.6 ± 0.4	1.4 ± 0.2	1.7 ± 0.5	.187
Antiplatelet, n (%)	29 (11.6)	6 (10.0)	23 (12.1)	.657
Anticoagulant, n (%)	11 (4.4)	5 (8.3)	6 (3.2)	.140
Initial ICH volume	15.1 ± 1.2	19.9 ± 2.2	13.6 ± 1.4	<.001
Initial IVH, n (%)	99 (39.6)	35 (58.3)	66 (33.7)	<.001

aPTT = activated partial thromboplastin time, ICH = intracranial hemorrhage, INR = international normalized ratio, IVH = intraventricular hemorrhage, PT = prothrombin time.

2.3. Clinical data

Clinical and demographic data were acquired through a retrospective review of medical charts. The collected data included sex, age, underlying disease (hypertension, diabetes, chronic renal disease, liver disease, or cardiac disease), smoking, alcohol consumption, previous medication, and initial GCS for correlation between hematoma expansion and NCCT and CTA imaging findings.

2.4. Image analysis

Initial NCCT for the diagnosis of BHS, IS, SS, BS, and CTA for the diagnosis of spot signs were reviewed retrospectively by 2 neuroradiologists with 25 and 15 years of experience, respectively. Two reviewers, without information on the study design, evaluated the anonymized and randomized images. Discrepancies regarding the diagnosis of the 4 NCCT markers and CTA spot signs were settled by a joint discussion of the reviewers.

The imaging findings of NCCT for the detection of ICH expansion have been considered in previous studies. The BHS (Fig. 1A) was defined as follows: a hypoattenuated and encapsulated area encapsulated within the high-density hematoma and a black hole with round, oval, or rod-like and no connection to the adjacent brain tissue, and the hematoma should have at least a 28 HU difference between the 2 density regions.[5,6] The hematoma IS on NCCT (Fig. 1B) is defined as ≥ 3 scattered and small hematomas, all separate from the main hematoma, or ≥ 4 small hematomas, some or all of which may connect with the main hematoma. The scattered small hematomas were round or oval and were separated from the main hematoma. The connected small hematomas should bebubble-or sprout-like.[7] The hematoma SS (Fig. 1C) on NCCT was defined as an area of low density (30–50 HU, hypo- or isodense to the brain parenchyma) surrounded by a hyperdense fluid collection.[8,9] Hematoma BS (Fig. 1D) represents a hematoma with a hyperdense and hypodense area and a well-defined margin that is recognized by the eye. The 2 different regions showed a difference of at least 18 HU. The hypodense area should not be encapsulated by ICH.[10,11] The spot sign on CTA (Fig. 1E) was defined as the presence of at least 1 focus of contrast density within the ICH, with a lack of connection with normal or abnormal vessels surrounding the hemorrhage, and without hyperdensity at the corresponding location on NCCT.[12–14] Reviewers reviewed by consensus and rated the presence of 4 NCCT markers and CTA spot sign based on a 4-point scoring system, where a score of 4 indicated they were "completely confident," 3 "probably confident," 2 "less confident," and 1 if they could not detect the imaging finding. The reviewers evaluated the NCCT or CTA within a 4-weeks interval.

Another reviewer measured the ICH volume on initial and follow-up NCCT in millimeters using the ABC/2 method.[15,16] An increase of hematoma size > 33% or > 6 mL was considered significant enlargement.[17,18]

Table 2

Comparison of NCCT and CTA for patients with and without ICH expansion.

	Total (n = 250)	ICH expansion (n = 60)	No expansion (n = 190)	*P*
Black hole sign, n (%)	118 (47.2)	31 (51.7)	87 (45.8)	.427
Blend sign, n (%)	52 (20.8)	16 (26.7)	36 (18.9)	.199
Island sign, n (%)	93 (37.2)	28 (46.7)	65 (34.2)	.082
Swirl sign, n (%)	79 (31.6)	31 (51.7)	48 (25.3)	<.001
Spot sign, n (%)	56 (22.4)	44 (73.3)	12 (6.3)	<.001

CTA = CT angiography, ICH = intracranial hemorhage, NCCT = non-contrast CT.

2.5. Statistical analysis

Continuous variables were summarized as means with standard deviations, while categorical data were expressed as counts and percentages. To assess the diagnostic accuracy of the imaging markers on NCCT or CTA for ICH expansion, an alternative free-response receiver operating characteristic (ROC) curve analysis was performed based on a 4-point scoring system by consensus of the reviewers. The diagnostic accuracy of each imaging marker was assessed by calculating the area under the alternative free response ROC curve (Az). The differences between the imaging markers with regard to the area under the ROC curves were statistically analyzed using the 2-tailed Student *t* test for paired data. The sensitivities and positive predictive values for each observer and each imaging modality were also calculated based on the number of lesions assigned a confidence level of 3 or 4 from among all lesions. The sensitivity and positive predictive value of each imaging marker were compared using McNemar's test. The significance level for the statistical analysis was set at $P < .05$.

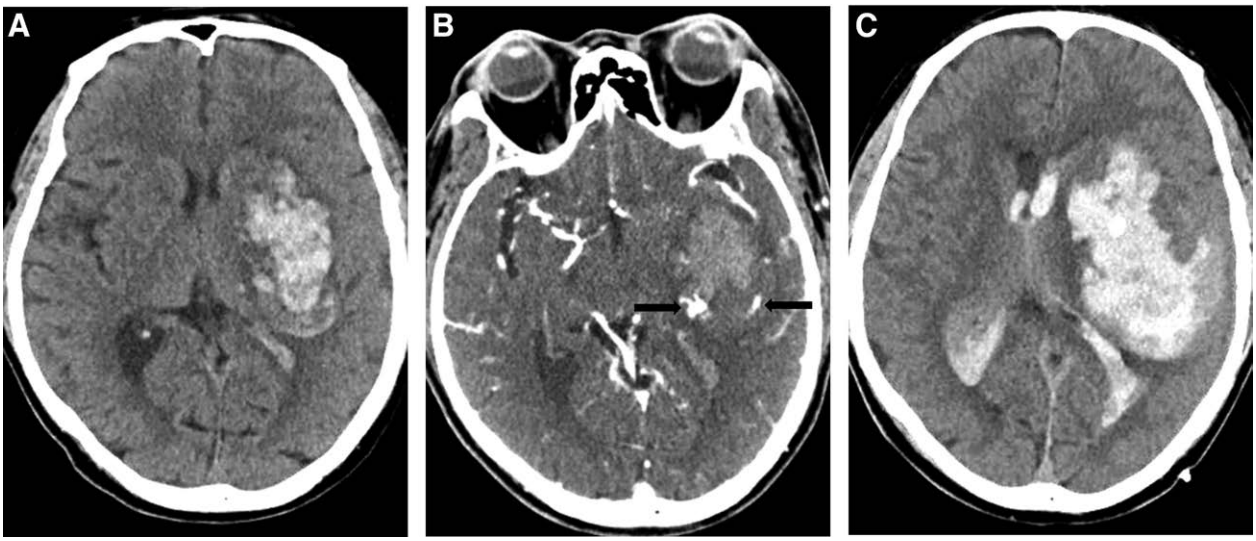

Figure 2. (A). Initial noncontrast computed tomography (CT) of a 66-year-old man demonstrates hyperdense hematoma in the left basal ganglia. Note positive findings of black hole sign, island sign, and swirl sign. (B). CT angiography demonstrates hyperdense spot signs in the hematoma (arrows). (C). Follow-up CT scan performed 2 h later demonstrates increased hematoma volume.

Table 3

Univariate analysis of predictors of ICH expansion.

	OR	95%	*P*
Age	0.990	0.969–1.011	.343
Male, n (%)	1.111	0.622–1.986	.722
Hypertension, n (%)	0.763	0.424–1.371	.365
Diabetes, n (%)	0.953	0.481–1.888	.890
Smoking, n (%)	0.732	0.263–2.032	.549
Alcohol, n (%)	1.371	0.631–2.980	.425
Chronic renal disease, n (%)	1.867	0.527–6.612	.333
Liver disease, n (%)	1.636	0.536–4.991	.387
Systolic blood pressure	0.997	0.989–1.005	.496
PT	1.031	0.997–1.066	.072
aPTT	1.008	0.969–1.050	.682
INR	0.985	0.914–1.063	.704
Antiplatelet, n (%)	0.807	0.312–2.085	.658
Anticoagulant, n (%)	2.788	0.819–9.485	.101
ICH volume	1.015	1.001–1.029	.038
Black hoe sign, n (%)	1.266	0.708–2.263	.427
Blend sign, n (%)	1.556	0.790–3.063	.201
Island sign, n (%)	1.683	0.934–3.033	.083
Swirl sign, n (%)	3.162	1.731–5.799	<.001
Spot sign, n (%)	40.792	18.002–92.432	<.001
Initial IVH	2.756	1.520–4.997	<.001

aPTT = activated partial thromboplastin time, ICH = intracranial hemorrhage, INR = international normalized ratio, IVH = intraventricular hemorrhage, PT = prothrombin time.

Multivariate analysis of ICH expansion was performed using logistic regression analysis. Variables with $P < .20$ from univariate analysis were considered candidate predictors for multivariate analysis. The significance level for the statistical analysis was set at $P < .05$. Analyses were performed using SPSS v.24.0 for Windows (IBM, Somers, NY) and MedCalc v.11.6.0 for Windows (MedCalc Software, Mariakerke, Belgium).

3. Results

A total of 250 patients (mean age, 65.3 years; age range, 38–90 years; male, 52.0%) with spontaneous ICH and complete NCCT and CTA examination following our study protocol were enrolled in this study. Of these patients, 60 (24.0%) had ICH expansion on the immediate follow-up NCCT.

Table 4

Multivariate analysis of predictors of ICH expansion.

	OR	95%	*P*
ICH volume	1.006	0.986–1.027	.563
Island sign	0.510	0.190–1.368	.181
Swirl sign	0.308	0.093–1.025	.055
Spot sign	109.5	29.954–400.286	<.001
Anticoagulant	4.121	0.368–46.167	.251
PT	1.006	0.917–1.104	.895
Initial IVH	4.111	1.690–10.000	.002

ICH = intracranial hemorrhage, IVH = intraventricular hemorrhage, PT = prothrombin time.

The demographic characteristics of the patients with and without ICH expansion are summarized in Table 1. Initial ICH volume in patients with ICH expansion was significantly higher than that in patients without ICH expansion (19.9 ± 2.2 vs 13.6 ± 1.4, $P < .001$). The incidence of initial IVH in patients with ICH expansion was significantly higher than that in patients without ICH expansion (58.3% vs 33.7%, $P < .001$).

The results of the 4 NCCT markers and CTA spot signs in patients with and without ICH expansion are summarized in Table 2. SS on NCCT and spot sign on CTA were significantly more prevalent in patients with ICH expansion ($P < .001$) (Fig. 2).

Logistic regression was performed to assess the association between clinical data, radiologic markers, and ICH expansion. In univariate logistic regression, the initial ICH volume ($P = .038$), initial intraventricular hemorrhage (IVH) ($P < .001$), SS ($P < .001$), and spot sign ($P < .001$) were associated with ICH expansion (Table 3). Multivariable logistic regression analysis confirmed the presence of initial IVH (OR 4.111; $P = .002$) and CTA spot sign (OR 109.5; $P < .001$) as independent predictors of ICH expansion (Table 4).

The interpretation of NCCT and CTA findings and the sensitivity and specificity of ICH expansion in patients with abnormal CT findings are summarized in Table 5. The sensitivity, PPV, and NPV of the CTA spot sign were significantly higher than those of the 4 NCCT markers ($P < .05$). In univariate logistic regression, the initial ICH volume ($P = .038$), initial intraventricular hemorrhage (IVH) presence ($P < .001$), swirl sign ($P < .001$), and spot sign ($P < .001$) were associated with ICH expansion.

The specificity of the CTA spot sign in patients without ICH expansion was significantly higher than that of the 4 NCCT markers ($P < .001$).

The area under the ROC curves values between ICH expansion and NCCT and CTA imaging findings for both observers are summarized in Table 6. The area under the ROC curves for the CTA spot sign was significantly higher than that for the 4 NCCT markers ($P < .05$) (Fig. 3).

4. Discussion

Our results showed that the CTA spot sign had a significantly higher sensitivity and specificity in patients with ICH expansion, but the 4 NCCT markers had lower sensitivity for ICH expansion. In particular, only the CTA spot sign as an imaging marker independently contributed to the hematoma expansion.

Although spontaneous ICH comprises only 10% to 20% of all strokes, its mortality rates approach 30% to 40% at 1 month, and up to 75% of patients suffer significant disability or mortality at 1 year.[19–23] Currently, the management of spontaneous ICH patients includes primarily supportive therapies,[24] such as airway management, hemodynamic monitoring, and control of intracranial pressure,[25] with no treatment options demonstrating significant efficacy.[26] However, preventing secondary expansion of hemorrhage after initial ICH highlights opportunities for therapeutic intervention.[24] Such expansion occurs in approximately one-third of ICH patients and is associated with significantly worse clinical outcomes.[1,3,4,26–28] So, predicting secondary expansion may help to include as many patients as possible who need antiexpansion therapies, such as intensive blood pressure reduction or administration of tranexamic acid.[27,29–32]

The clinical value of NCCT markers and the CTA spot sign as predictors of ICH expansion has been validated in several studies.[5–14] He et al compared the black hole sign and other CT features (irregular hematoma and initial hematoma volume) to predict hematoma expansion and outcome.[5] They found that irregular hematoma, black hole sign on CT, and delayed intraventricular hemorrhage extension were independent predictors of hematoma expansion. The CT black-hole sign presented the highest accuracy in predicting hematoma expansion. However, it was not an independent predictor of poor outcome. Xin et al also reported the black hole sign to be a good predictor of hematoma growth.[6] Qi Li et al proposed the island sign as a reliable CT imaging marker that independently predicts hematoma expansion and poor outcomes in patients with ICH.[7] D. Ng et al demonstrated that the swirl sign is associated with a larger initial hematoma, earlier initial CT, and hematoma expansion.[8] Sporns et al identified hematoma volume, intraventricular hemorrhage, and the presence of a blended sign as independent predictors of neurological deterioration.[10] Those were studies on NCCT markers, and the following studies focused on the CTA spot sign. In a patient-level meta-analysis of studies reporting ICH growth, with data on over 5400 subjects by Al-Shahi Salman et al,[33] independent predictors of hemorrhage growth were time from symptom onset to baseline imaging, ICH volume on baseline imaging, antiplatelet use, anticoagulant use, and contrast extravasation ("spot sign") on initial CT angiography. Xu et al reported that the spot sign was related to an increased risk of hematoma expansion and had a significantly higher risk of in-hospital and 3-month death.[12] Also, Han et al identified that the spot sign is a strong independent predictor of hematoma expansion, mortality, and poor clinical outcomes in primary ICH. Morotti et al investigated whether the integration of spot signs and hypodensities improves the stratification of ICH expansion risk.[34] They showed that the spot sign and hypodensities predict hematoma growth independently from each other, and their integrated analysis identifies patients at the highest risk of ICH expansion. Hypodensity had a higher sensitivity for ICH expansion, whereas specificity was superior for the spot sign.

Recently, Sporns et al investigated the degree of interaction between 5 NCCT imaging markers (BS, BHS, IS, hypodensities, and heterogeneous densities) and the CTA spot sign and their individual contribution to outcome prediction in patients with ICH.[10] The CTA spot sign and NCCT hypodensities were the 2 most important independent risk factors for poor outcomes after ICH. However, our study focused on ICH expansion. The spot sign had the highest sensitivity and specificity among the imaging parameters.

Some limitations of this study should be considered when interpreting our results. Our study was a non-randomized, single-center, retrospective analysis. In addition, the sample size was relatively small. Another limitation is that our study lacks a long-term follow-up (such as the modified Rankin scale) that might offer additional information but was not available for this study. Additionally, the interobserver agreement of the NCCT island sign was relatively low compared with that of the other markers.

5. Conclusion

We demonstrated that only the CTA spot sign suggested a high risk of ICH expansion; in particular, the spot sign showed higher sensitivity and specificity for ICH expansion. Multivariate analysis showed that the presence of the CTA spot sign was independently correlated with hematoma expansion. Therefore, although contrast medium in CTA has some risks, such as allergic reaction or renal dysfunction, not only NCCT but also CTA should be performed if possible. This could allow for better

Table 6

ROC analysis of this study.

Variable	AUC	SE	95% CI
Black hole sign	0.529	0.047	0.461–0.596
Blend sign	0.569	0.041	0.501–0.635
Island sign	0.586	0.043	0.518–0.651
Swirl sign	0.601	0.048	0.534–0.666
Spot sign*	0.733	0.040	0.670–0.79

AUC = area under the ROC curves.

*AUC of CTA spot sign was significantly higher than that of 4 NCCT markers ($P < .05$).

Table 5

Sensitivity and specificity of 4 NCCT markers and the CTA spot sign associated with ICH expansion.

	BHS (n = 118)	BS (n = 52)	IS (n = 93)	SS (n = 79)	Spot sign (n = 56)
Sensitivity,%	26.3	30.8	30.1	39.2	78.6*
Specificity,%	78.0	77.8	79.6	83.0	91.8**
PPV,%	51.7	26.7	46.7	51.7	73.3*
NPV,%	54.2	81.1	65.8	74.7	93.7*

*CTA spot sign was significantly higher than that of 4 NCCT markers ($P < .001$).

**CTA spot sign was significantly higher than that of BHS, BS, and IS ($P < .05$).

BHS = black hole sign, BS = Blend sign, IS = island sign, NPV = negative predictive value, PPV = positive predictive value, SS = swirl sign.

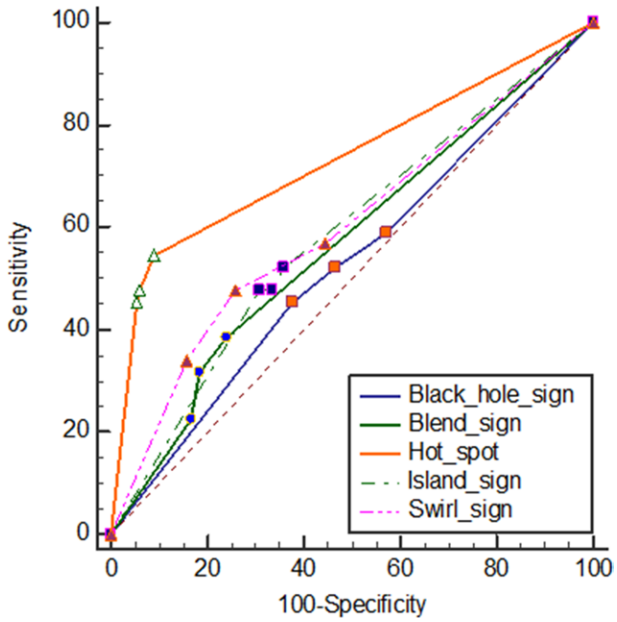

Figure 3. ROC curve. The AUC of the CTA spot sign was significantly higher than that of the 4 NCCT markers. AUC = area under the ROC curves, CTA = computed tomographic angiography, NCCT = noncontrast computed tomography, ROC = receiver operating characteristic curve.

prediction of expansion than NCCT imaging markers alone, and may help set a potential therapeutic target for anti-expansion treatment in the future.

Acknowledgments

We thank Emareye Medical Editing (emareye.com) for the English language editing.

Author contributions

Conceptualization: Hyo Sung Kwak.
Data curation: Ja Hong Goo.
Formal analysis: Ja Hong Goo, Hyo Sung Kwak, Seung Bae Hwang, Gyung Ho Chung.
Funding acquisition: Hyo Sung Kwak.
Writing – original draft: Ja Hong Goo, Gyung Ho Chung.
Writing – review & editing: Hyo Sung Kwak.

References

[1] Brott T, Broderick J, Kothari R, et al. Early hemorrhage growth in patients with intracerebral hemorrhage. Stroke. 1997;28:1–5.
[2] Li Q, Shen YQ, Xie XF, et al. Expansion-prone hematoma: defining a population at high risk of hematoma growth and poor outcome. Neurocrit Care. 2019;30:601–8.
[3] Davis SM, Broderick J, Hennerici M, et al. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. Neurology. 2006;66:1175–81.
[4] Delcourt C, Huang Y, Arima H, et al. Hematoma growth and outcomes in intracerebral hemorrhage: the INTERACT1 study. Neurology. 2012;79:314–9.
[5] He GN, Guo HZ, Han X, et al. Comparison of CT black hole sign and other CT features in predicting hematoma expansion in patients with ICH. J Neurol. 2018;265:1883–90.
[6] Xiong X, Li Q, Yang WS, et al. Comparison of Swirl Sign and Black Hole Sign in predicting early hematoma growth in patients with spontaneous intracerebral hemorrhage. Med Sci Monit. 2018;24:567–73.
[7] Li Q, Liu QJ, Yang WS, et al. Island sign: an imaging predictor for early hematoma expansion and poor outcome in patients with intracerebral hemorrhage. Stroke. 2017;48:3019–25.
[8] Ng D, Churilov L, Mitchell P, et al. The CT Swirl sign is associated with hematoma expansion in intracerebral hemorrhage. AJNR Am J Neuroradiol. 2018;39:232–7.
[9] Al-Nakshabandi NA. The swirl sign. Radiology. 2001;218:433.
[10] Sporns PB, Schwake M, Kemmling A, et al. Comparison of spot sign, blend sign and black hole sign for outcome prediction in patients with intracerebral hemorrhage. J Stroke. 2017;19:333–9.
[11] Li Q, Zhang G, Huang YJ, et al. Blend sign on computed tomography: novel and reliable predictor for early hematoma growth in patients with intracerebral hemorrhage. Stroke. 2015;46:2119–23.
[12] Xu X, Zhang J, Yang K, et al. Accuracy of spot sign in predicting hematoma expansion and clinical outcome: a meta-analysis. Medicine (Baltim). 2018;97:e11945.
[13] Wada R, Aviv RI, Fox AJ, et al. CT angiography "spot sign" predicts hematoma expansion in acute intracerebral hemorrhage. Stroke. 2007;38:1257–62.
[14] Han JH, Lee JM, Koh EJ, et al. The spot sign predicts hematoma expansion, outcome, and mortality in patients with primary intracerebral hemorrhage. J Korean Neurosurg Soc. 2014;56:303–9.
[15] Divani AA, Majidi S, Luo X, et al. The ABCs of accurate volumetric measurement of cerebral hematoma. Stroke. 2011;42:1569–74.
[16] Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. Stroke. 1996;27:1304–5.
[17] Demchuk AM, Dowlatshahi D, Rodriguez-Luna D, 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;11:307–14.
[18] Dowlatshahi D, Demchuk AM, Flaherty ML, et al. Defining hematoma expansion in intracerebral hemorrhage: relationship with patient outcomes. Neurology. 2011;76:1238–44.
[19] Ikram MA, Wieberdink RG, Koudstaal PJ. International epidemiology of intracerebral hemorrhage. Curr Atheroscler Rep. 2012;14:300–6.
[20] Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. Lancet. 2009;373:1632–44.
[21] van Asch CJ, Luitse MJ, Rinkel GJ, et al. 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;9:167–76.
[22] Anderson CS, Huang Y, Wang JG, et al. Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. Lancet Neurol. 2008;7:391–9.
[23] VanDerWerf J, Kurowski D, Siegler J, et al. Combination of intra-hematomal hypodensity on CT and BRAIN scoring improves prediction of hemorrhage expansion in ICH. Neurocrit Care. 2018;29:40–6.
[24] Belur PK, Chang JJ, He S, et al. Emerging experimental therapies for intracerebral hemorrhage: targeting mechanisms of secondary brain injury. Neurosurg Focus. 2013;34:E9.
[25] Babu R, Bagley JH, Di C, et al. Thrombin and hemin as central factors in the mechanisms of intracerebral hemorrhage-induced secondary brain injury and as potential targets for intervention. Neurosurg Focus. 2012;32:E8.
[26] Brouwers HB, Greenberg SM. Hematoma expansion following acute intracerebral hemorrhage. Cerebrovasc Dis. 2013;35:195–201.
[27] Boulouis G, Morotti A, Goldstein JN, et al. Intensive blood pressure lowering in patients with acute intracerebral haemorrhage: clinical outcomes and haemorrhage expansion. Systematic review and meta-analysis of randomised trials. J Neurol Neurosurg Psychiatry. 2017;88:339–45.
[28] Fujii Y, Tanaka R, Takeuchi S, et al. Hematoma enlargement in spontaneous intracerebral hemorrhage. J Neurosurg. 1994;80:51–7.
[29] Qureshi AI, Palesch YY, Barsan WG, et al. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. N Engl J Med. 2016;375:1033–43.
[30] Anderson CS, Heeley E, Huang Y, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med. 2013;368:2355–65.
[31] Sprigg N, Renton CJ, Dineen RA, et al. Tranexamic acid for spontaneous intracerebral hemorrhage: a randomized controlled pilot trial (ISRCTN50867461). J Stroke Cerebrovasc Dis. 2014;23:1312–8.
[32] Cao D, Li Q, Fu P, et al. Early hematoma enlargement in primary intracerebral hemorrhage. Curr Drug Targets. 2017;18:1345–8.
[33] Al-Shahi Salman R, Frantzias 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;17:885–94.
[34] Morotti A, Boulouis G, Charidimou A, et al. Integration of computed tomographic angiography spot sign and noncontrast computed tomographic hypodensities to predict hematoma expansion. Stroke. 2018;49:2067–73.