Clinical Neurology and Neurosurgery 182 (2019) 130–135

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Diagnostic value of swirl sign on noncontrast computed tomography and spot sign on computed tomographic angiography to predict intracranial hemorrhage expansion

Bo Kyoung Park[a], Hyo Sung Kwak[b,*], Gyung Ho Chung[b], Seung Bae Hwang[b]

[a] Chonbuk National University Medical School, Republic of Korea

[b] Department of Radiology and Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, Republic of Korea

A R T I C L E I N F O

Keywords:
Cerebral hemorrhage
Computed tomographic angiography
Hematoma expansion
Noncontrast computed tomography

A B S T R A C T

Objective: Intracranial hemorrhage (ICH) expansion is a predictor of poor clinical outcome. ICH expansion can be predicted with a swirl sign on noncontrast computed tomography (NCCT) and/or a spot sign on computed tomographic angiography (CTA). In this study, we aimed to evaluate the diagnostic value of a swirl sign and a spot sign in identifying hematoma expansion.

Patients and methods: Patients with spontaneous ICH between January 2013 and August 2018 who underwent an initial NCCT and CTA, and a subsequent NCCT at a single center were retrospectively identified. Two experienced neuroradiologists reviewed all images for swirl sign and spot sign presence using a 4-point scale for receiver-operative characteristic analysis. ICH expansion was defined as volume growth of > 33% or > 6 mL.

Results: A total of 227 patients, including 54 with ICH expansion, qualified for analysis. For both observers, the area under the curve (AUC) of spot sign was significantly higher than that of swirl sign (observer 1: 0.748 vs. 0.577, p = .002; observer 2: 0.749 vs. 0.589, p = .004). The sensitivities of ICH expansion in patients with a spot sign was significantly higher than patients with a swirl sign (observer 1: 54.1% vs. 28.0%, p = .002; observer 2: 56.9% vs. 30.3%, p = .002). Patients with a spot sign had the highest risk of ICH expansion (odds ratio: observer 1 = 8.14, observer 2 = 9.30, p < 0.001).

Conclusions: A spot sign on CTA was identified and associated with ICH expansion. A swirl sign on NCCT had a relatively low sensitivity and AUC, and will not be able to replace spot sign on CTA.

1. Introduction

Intracerebral hemorrhage (ICH) is known to have dire prognosis, proven by its high 30-day mortality rate of approximately 40% [1]. To predict patient's poor functional outcome and mortality, hematoma expansion is used as an independent determinant [1,2]. Almost 40% of ICH patients showed hematoma expansion on the first day of symptom onset [3].

Prognostic factors of ICH included initial volume, age, low Glasgow Coma Scale (GCS) score, and shorter time from onset to presentation [4,5]. ICH expansion due to active rebleeding or extravasation has been reported in 38–70% of patients during the first 24 h after symptom onset [6,7]. Especially, ICH expansion is associated with early neurologic deterioration and is an independent predictor of poor clinical outcome and increased morbidity [7–10]. CT protocol in patients with ICH had purposed the evaluation of initial volume, location, and prevalence of ICH expansion. A spot sign on CTA is a potent imaging marker that is associated with early ICH expansion [3,11–13]. Recently, NCCT markers such as blend sign, black hole sign, swirl sign, and island sign were proposed for predicting ICH expansion [14–17]. A swirl sign on NCCT is a hypo- or iso-attenuated lesion within a hyper-attenuated fluid collection [18]. The spot sign identification requires performing early CTA examination which is not routinely executed in many institutions [19,20]. Furthermore, diagnostic criteria of imaging findings of spot sign/swirl sign have been proposed with great heterogeneity [21].

Some papers reported the relationship between imaging findings of CTA and NCCT and ICH expansion [22,23]. The combined analysis of hypodensity on NCCT and spot sign on CTA improved the stratification of ICH expansion risk [23]. In this study, we aimed to evaluate the

* Corresponding author at: Radiology and Research Institute of Clinical Medicine of Chonbuk National University-Biomedical Research Institute of Chonbuk National University Hospital, 567 Baekje-daero, deokjin-gu, Jeonju-si, Jeollabuk-do, 561-756, Republic of Korea.

E-mail address: kwak8140@jbnu.ac.kr (H.S. Kwak).

https://doi.org/10.1016/j.clineuro.2019.05.013
Received 16 March 2019; Received in revised form 10 May 2019; Accepted 13 May 2019
Available online 14 May 2019

diagnostic value of swirl sign and spot sign in better identifying hematoma expansion in patients with ICH by receiver-operative characteristic analysis.

2. Patients and methods

The study protocol was approved by our institutional review board. Informed consent was waived from relatives of the deceased.

2.1. Patients

This was a retrospective analysis of our institutional data of all patients who were admitted for treatment of ICH from January 2013 to August 2018. During this period, 345 patients were admitted for treatment of ICH. Inclusion criteria of this study were as follows: 1) age ≥ 18 years; 2) spontaneous ICH on history; 3) immediate NCCT within one hour after symptom onset; 4) CTA examination within one hour after NCCT; and 5) Follow-up NCCT examination between 2 and 6 h after CTA. Our exclusion criteria for this study were as follows: 1) brainstem or cerebellar hemorrhage; 2) trauma-related hemorrhage; 3) secondary ICH such as tumor, vasculitis, moyamoya disease, and venous infarction; 4) previous lobar infarction history; and 5) previous brain surgery history. Of 345 patients, 227 with spontaneous ICH and complete NCCT and CTA examination of our study protocol were enrolled in this study.

2.2. CT acquisition

Initial NCCT (Definition Flash; Siemens, Erlangen, Germany) with a slice thickness of ≤5 mm were obtained for all patients. Patients in our sample had a NCCT, followed by a CTA if it was detected with ICH, which was performed by scanning from the cerebral vertex to the aortic arch with 0.7-mm section thickness slices. Nonionic contrast media (80–120 ml) was administered into the antecubital vein at 3–5 milliliters/second, and the CTA source images for 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 ≤5 mm was performed except for patients who needed emergency operation.

2.3. Clinical data

Clinical and demographic data were acquired through retrospective review of medical charts. The collected data included sex, age, underlying disease, previous medication, and initial GCS for correlation between hematoma expansion and imaging findings of NCCT and CTA.

2.4. Image analysis

Initial NCCT for diagnosis of swirl sign and CTA for diagnosis of spot sign were reviewed retrospectively by two neuroradiologists with 25 and 15 years of experience, respectively. They were not informed about the composition of the patient population and independently evaluated the anonymized, randomized images. The swirl sign on NCCT was defined as an area of low density (30–50 HU, hypo- or isodense to brain parenchyme) surrounded by a hyperdense fluid collection [17,18]. The spot sign on CTA was defined as presence of at least one focus of contrast density within the ICH, with lack of connection with normal or abnormal vessels surrounding the hemorrhage, and without hyper density at the corresponding location on NCCT [23,24]. Reviewers separately reviewed NCCT and CTA by standard radiological viewing, and rated the presence of spot sign or swirl sign finding based on a 4-point scoring system, where a score of 4 indicated they were "completely confident" about detecting the Spot sign or swirl sign, 3 "probably confident," 2 "less confident," and 1 if they could not detect the spot sign or swirl sign. Each observer has evaluated the NCCT or CTA with 4-weeks interval.

Another reviewer measured the volume of ICH of initial and follow-up NCCT in millimeters using the ABC/2 method [25]. An increase of hematoma size > 33% or > 6 mL was considered significant enlargement [6,8,12,26].

2.5. Statistical analysis

The correlation between ICH expansion and imaging findings of NCCT or CTA was assessed by calculating the area under the ROC curves (AUC). Differences between mean AUC were compared using two-tailed student's *t*-tests for paired data. Sensitivities for each observer and imaging set were evaluated according to the number of lesions assigned confidence levels of 3 or 4. Prior to image interpretation, observers were aware that lesions assigned confidence levels of 3 or 4 would be included in separate sensitivity calculations. Sensitivities were compared using McNemar's test. A two-tailed $p < 0.05$ was considered statistically significant. We also calculated 95% confidence intervals. We evaluated differences between these two groups using the Student *t*-test for continuous variables and the Fisher test for categorical variables.

To assess interobserver agreement, we calculated the κ statistic for both observers. The significance of the difference between the κ-values assigned to the two imaging modalities was then tested using z-tests. The statistical significance level was set at $p < 0.05$. Statistical analyses were performed using SPSS v. 22.0 for Windows (IBM, Somers, NY, USA) and Medcalc v.11.6.0 for Windows (MedCalc Software, Mariakerke, Belgium).

3. Results

A total 227 (median age, 63.5 years; age range, 32–90 years; male, 58.1%) with spontaneous ICH and complete NCCT and CTA examination of our study protocol were enrolled in this study. Of these patients, 54 (23.8%) had ICH expansion on immediate follow-up NCCT.

The demographic characteristics of patients with and without ICH expansion are summarized in Table 1. Of total patients, 126 (55.5%) had hypertension. Initial ICH volume in patients with ICH expansion was significantly higher than that in patients without ICH expansion (43.2 ± 33.2 vs. 32.8 ± 29.3, $p =$ 0.029). However, initial GCS in patients without ICH expansion was significantly higher than that in patients with ICH expansion (12.3 ± 3.5 vs. 10.7 ± 4.1, $p =$ 0.006).

Interpretation of CT findings and sensitivity of ICH expansion in patients with abnormal CT findings are summarized in Table 2. The swirl sign on NCCT in both observers was found approximately 33%. Of these patients, ICH expansion was appeared 28% in observer 1 and 30% in observer 2. The spot sign on CTA in both observers was found

Table 1
Demographic findings of two groups.

	ICH expansion (n = 54)	No ICH expansion (n = 173)	p value
Age	62.0 ± 14.4	64.0 ± 14.3	0.371
Male (%)	34 (63.0)	98 (56.6)	0.434
Hypertension (%)	29 (53.7)	97 (56.1)	0.757
Diabetes (%)	15 (27.8)	34 (19.7)	0.255
Chronic renal disease (%)	15 (27.8)	29 (16.8)	0.075
Liver disease (%)	13 (24.1)	25 (14.5)	0.096
Cardiac disease (%)	4 (7.4)	18 (10.4)	0.608
Previous stroke history (%)	11 (20.4)	18 (10.4)	0.064
Antiplatelet drug (%)	14 (25.9)	45 (26.0)	1.000
Anticoagulant drug (%)	4 (7.4)	6 (3.5)	0.057
GCS	10.7 ± 4.1	12.3 ± 3.5	0.006
ICH volume	43.2 ± 33.2	32.8 ± 29.3	0.029

Note – ICH, intracerebral hemorrhage; GCS, Glasgow Coma Scale.

Table 2
Sensitivity between ICH expansion and CT imaging findings of two observers.

	ICH expansion
Observer 1	
Swirl sign (n = 75)	21 (28.0%)
Spot sign (n = 61)	33(54.1%)[a]
Both (n = 31)	12 (38.7%)
Observer 2	
Swirl sign (n = 76)	23 (30.3%)
Spot sign (n = 58)	33 (56.9%)[a]
Both (n = 29)	12 (41.4%)

Note – ICH, intracerebral hemorrhage.
[a] Correlation of both observers between ICH expansion and spot sign were significantly higher than that between ICH expansion and swirl sign ($p = 0.002$).

Table 3
Receiver operative characteristic analysis between ICH expansion and CT imaging findings of two observers.

	Observer 1		Observer 2	
	Swirl sign	Spot sign	Swirl sign	Spot sign
AUC	0.577	0.748[a]	0.589	0.749[a]
95% CI	0.509 – 0.642	0.686 – 0.803	0.522 – 0.653	0.687 – 0.804
Z statistic	1.908	6.755	2.168	6.806
SD	0.040	0.037	0.041	0.037

Note – ICH, intracerebral hemorrhage; AUC, area under the ROC curve.
[a] AUC of both observers between ICH expansion and spot sign were significantly higher than that between ICH expansion and swirl sign ($p < 0.05$).

approximately 26–27%. Of these patients, ICH expansion was appeared 54% in observer 1 and 57% in observer 2. Positive findings of swirl sign and spot sign were found approximately 13%. ICH expansion appeared 39% in observer 1 and 41% in observer 2. Sensitivities of data between ICH expansion and spot sign on CTA was significantly higher than the data between ICH expansion and swirl sign on NCCT in both observers ($p = 0.002$) (Fig. 1).

The AUC values between ICH expansion and CT imaging findings in both observers are summarized in Table 3. For both observers, the AUC of spot sign was significantly higher than that of swirl sign (observer 1: 0.748 vs. 0.577, p = .002; observer 2: 0.749 vs. 0.589, $p = .002$) (Fig. 2). The Odds ratio between ICH expansion and CT imaging findings in both observers are summarized in Table 4. Patients with a spot sign had the highest risk of ICH expansion (odds ratio: observer 1 = 8.14, observer 2 = 9.30, $p < 0.001$).

The κ-values for the two observers between ICH expansion and CT imaging findings are summarized in Table 5. The κ-values were 0.795 for swirl sign on NCCT and 0.957 for spot sign on CTA, indicating excellent interobserver agreement. The κ-values of spot sign on CTA between two observers were significantly higher than that of swirl sign on NCCT ($p < 0.05$).

4. Discussion

The main finding of this retrospective study is that spot sign on CTA is the significant predictor of ICH expansion compared with swirl sign on NCCT. The spot sign has more interobserver agreement compared with swirl sign for interpretation of CT findings.

ICH expansion occurs in up to 70% of patients documented by NCCT performed within 3 h after onset of symptoms [6,27]. Unfortunately, treatment for ICH is not clearly established. The dire prognosis of ICH calls for a more effective and innovative treatment to be developed. Previous main predictors of early higher mortality and poor clinical outcome during the early phase of ICH are hematoma expansion, initial ICH volume, GCS, and IVH [7,8,28]. At least 38–70% of patients had > 33% growth in the volume of ICH during the first 24 h after symptom onset [6,7]. Hematoma volume increase of 10.7 ml (1 standard deviation) over 24 h had strong correlation with poor outcome [2]. Increased risk of major disability and death is associated with the speed of ultraearly ICH expansion in ICH patients [29]. Therefore, we defined that increase of hematoma size > 33% or > 6 mL was considered significant enlargement, retrospectively [8,26].

The mechanism of acute phase ICH expansion is not clearly understood. Mayer et al. [30,31] suggested that damage of the normal cerebral anatomy, collapse of blood-brain barrier, early transient ischemia, local tissue distortion, vascular engorgement caused by decrease of venous outflow, and rapid increase in ICP may result in hematoma expansion. Risk factors identified for ICH expansion include blood pressure, and vascular and coagulation disorders [11,32].

Early CT protocol in patients with ICH used either only NCCT or CTA after initial NCCT for evaluation of critical imaging findings of ICH expansion. The spot sign on CTA, also known as small, focal contrast enhancement within an intracerebral hematoma due to contrast extravasation, is a potent imaging marker that is associated with early ICH expansion and poor functional outcome in patients with ICH [3,11–13]. Recently, NCCT markers such as blend sign, black hole sign, swirl sign, and island sign were proposed for predicting ICH expansion [14–17]. Swirl sign on NCCT is a hypo- or iso-attenuated lesion within a hyper-

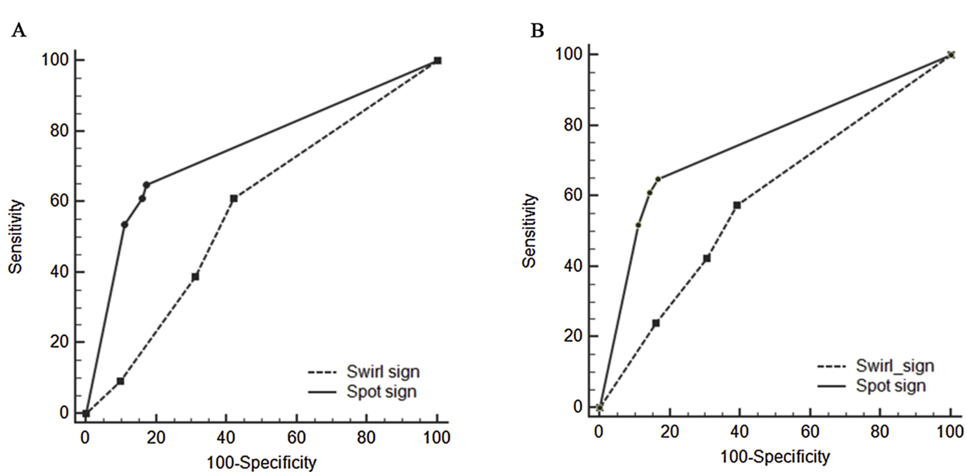

Fig. 1. ROC Curve.
A.ROC curve of observer 1. B. ROC curve of observer 2. The AUC of spot sign was significantly higher than that of swirl sign.

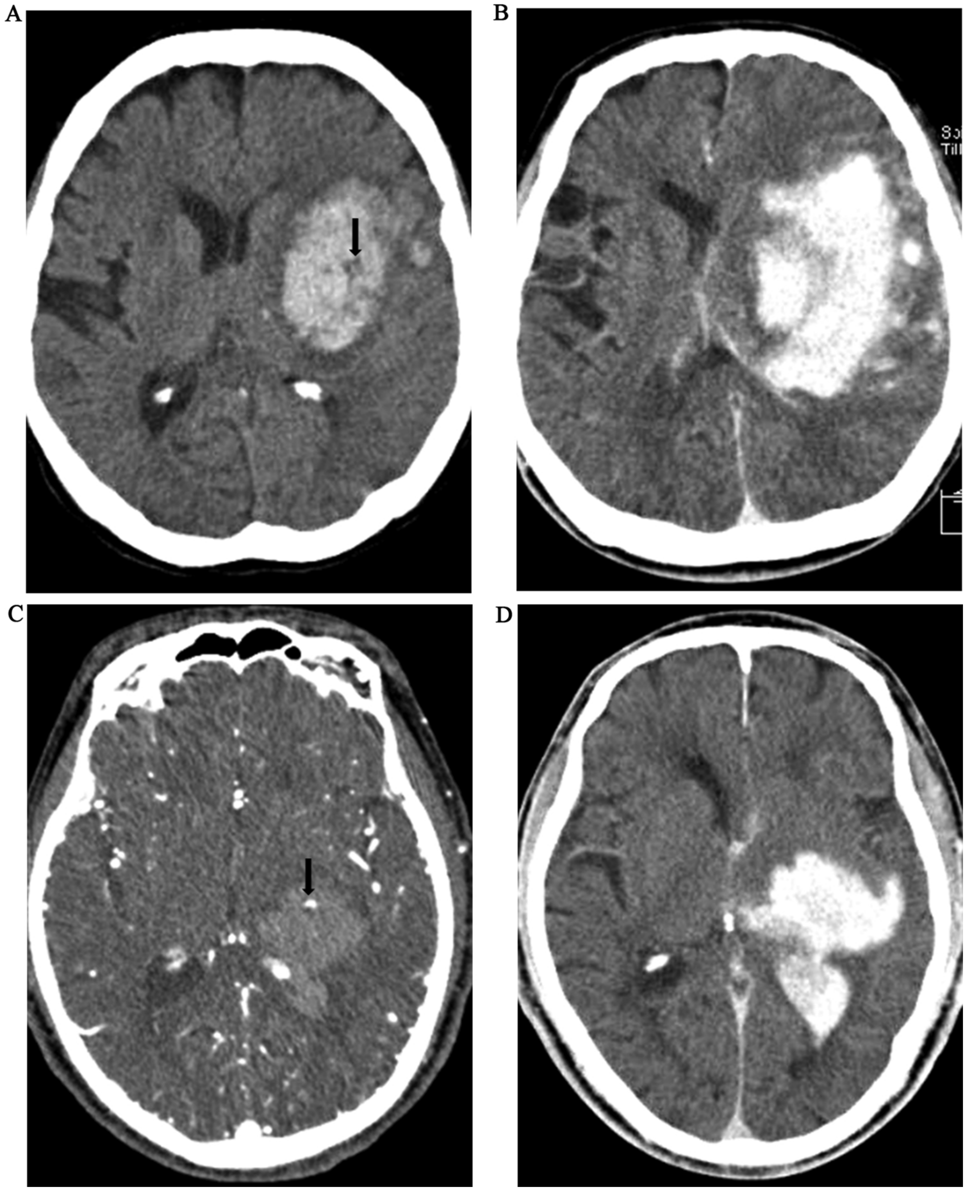

Fig. 2. ICH expansion.
A and B. Swirl sign. A. Noncontrast CT of a 73-year-old woman demonstrates hyperdense hematoma with hypodense foci (arrow). B. Follow-up CT scan performed 2 h later demonstrates increased hematoma volume.
C and D. Spot sign. A. Initial CTA of a 81-year-old man demonstrates hyperdense foci in the initial ICH (arrow). B. Follow-up CT scan performed 2 h later demonstrates increased hematoma volume.

Table 4
Odds ratio between ICH expansion and CT imaging findings of two observers.

	Observer 1		Observer 2	
	Swirl sign	Spot sign	Swirl sign	Spot sign
Odds ratio	1.402	8.138	1.680	9.303
95% CI	0.743 – 2.645	4.121 – 16.071	0.896 – 3.151	4.656 – 18.586
z statistic	1.044	6.039	1.617	6.316
Significance level	P = 0.296	P < 0.000	P = 0.106	P < 0.000

Note – ICH, intracerebral hemorrhage.

Table 5
Kappa value of CT imaging findings of two observers.

	Swirl sign	Spot sign[a]
Kappa	0.795	0.957
Standard error	0.023	0.0127
95% CI	0.751 – 0.840	0.9327 – 0.9817

[a] Kappa values of spot sign between two observers were significantly higher than that of swirl sign ($p < 0.05$).

attenuated fluid collection [18]. Especially, the sensitivity of imaging markers on NCCT is relatively low.

Some papers reported the relationship between imaging findings of CTA and NCCT and ICH expansion [22,23]. Sporns et al. [22] reported the correlation between blend sign on NCCT and spot sign on CTA in patients with secondary neurological deterioration after spontaneous ICH. Of the 81 patients with secondary deterioration, 31 (38.3%) had blend sign and spot sign on admission. The CT blend sign showed a high association with the CTA spot sign and was a reliable predictor of secondary neurological deterioration after spontaneous ICH. When included in the multivariable analysis, the spot sign was no longer as a significant predictor of secondary neurological deterioration. Also, this paper analyzed the correlation between imaging findings and secondary neurological deterioration instead of ICH expansion in patients with spontaneous ICH. The combination of the two radiological signs does not improve the prediction of hematoma growth in patients with spontaneous ICH. Morotti et al. [23] investigated whether the integration of spot sign and hypodensity improved the stratification of ICH expansion risk. The rate of ICH expansion was 55.6% in patients with both spot sign on CTA and hypodensity on NCCT. Subjects with both imaging findings on CT had the highest risk of hematoma growth (odds ratio, 9.50). In our study, spot sign on CTA in patients with ICH expansion by each observer had significantly higher prevalence than swirl sign on NCCT. Also, positive findings of swirl sign and spot sign in patients with ICH expansion was appeared 39% in observer 1 and 41% in observer 2. This ratio was relatively low compared with only spot sign. Our results revealed some difference compared with previous reports [22,23]. Our results reflected the high detection of swirl sign on NCCT and relatively low correlation to ICH expansion.

Xu et al. [33] reported the meta-analysis about accuracy of spot sign in predicting hematoma expansion and clinical outcome. The spot sign occurred in 23.4% patients with spontaneous ICH and was related with approximately 8-fold increased risk of ICH expansion [33]. Also, patients with spot sign had a significantly higher risk of in-hospital death and 3-month death. In our study, the spot sign was related with approximately 8- or 9-fold increased risk of ICH expansion. However, the swirl sign did not show the relation of ICH expansion.

Also, in the present study, the diagnostic accuracy (AUC) of spot sign on CTA for relation of ICH expansion by both observers was significantly higher than that of swirl sign on NCCT. Interobserver agreement of swirl sign on NCCT was significantly lower than that of spot sign on CTA. The results of the present study suggest that the swirl sign on NCCT without CTA as single marker for ICH expansion would have a limited role because of lower sensitivity and relatively low interobserver agreement. Our study results show spot sign in CTA have higher AUC, sensitivities and risk of ICH expansion. These results support the decision to routinely give contrast media and perform CTA in patients presenting with ICH.

This study has some limitations. First, only a relatively small number of cases with retrospective nature and single center design were evaluated. A larger number of cases and longitudinal prospective studies are needed to validate our results. Second, our study only included the swirl sign without blend sign or black hole sign on NCCT. Therefore, correlation of ICH expansion and swirl sign on NCCT could be led to potential underestimation. However, in our study, interobserver agreement of swirl sign on NCCT was relatively low. Spot sign on CTA was more valuable in terms of the diagnostic accuracy of imaging finding associated with ICH expansion Finally, we analyzed the imaging findings related to ICH expansion. Therefore, we did not includ the results about mortality or clinical outcome of various clinical data.

5. Conclusion

Spot sign on CTA was identified and associated with ICH expansion, supporting the decision to routinely perform CTA in patients presenting with ICH. Swirl sign on NCCT has a relatively low sensitivity and AUC, and will not be able to replace spot sign. Also, spot sign on CTA has higher interobserver agreement by observers. Therefore, spot sign on CTA may need the selection of patients for antiexpansion treatments in acute state and for clinical trials testing antiexpansion treatments.

Funding

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2017R1D1A3B03032390).

Competing interests

None.

Ethical approval

Our institutional review board approved this retrospective study.

References

[1] J.P. Broderick, T. Brott, T. Tomsick, R. Miller, G. Huster, Intracerebral hemorrhage more than twice as common as subarachnoid hemorrhage, J. Neurosurg. 78 (2) (1993) 188–191.
[2] C. Delcourt, Y. Huang, H. Arima, J. Chalmers, S.M. Davis, E.L. Heeley, J. Wang, M.W. Parsons, G. Liu, C.S. Anderson, Hematoma growth and outcomes in intracerebral hemorrhage: the INTERACT1 study, Neurology 79 (4) (2012) 314–319.
[3] A.M. Demchuk, D. Dowlatshahi, D. Rodriguez-Luna, C.A. Molina, Y.S. Blas, I. Dzialowski, A. Kobayashi, J.M. Boulanger, C. Lum, G. Gubitz, V. Padma, J. Roy, C.S. Kase, J. Kosior, R. Bhatia, S. Tymchuk, S. Subramaniam, D.J. Gladstone, M.D. Hill, R.I. Aviv, Prediction of haematoma growth and outcome in patients with intracerebral haemorrhage using the CT-angiography spot sign (PREDICT): a prospective observational study, Lancet Neurol. 11 (4) (2012) 307–314.
[4] J.C. Hemphill 3rd, D.C. Bonovich, L. Besmertis, G.T. Manley, S.C. Johnston, The ICH score: a simple, reliable grading scale for intracerebral hemorrhage, Stroke 32 (4) (2001) 891–897.
[5] S. Curtze, D. Strbian, A. Meretoja, J. Putaala, H. Eriksson, E. Haapaniemi, S. Mustanoja, T. Sairanen, J. Satopaa, H. Silvennoinen, M. Niemela, M. Kaste, T. Tatlisumak, Higher baseline international normalized ratio value correlates with higher mortality in intracerebral hemorrhage during warfarin use, Eur. J. Neurol. 21 (4) (2014) 616–622.
[6] T. Brott, J. Broderick, R. Kothari, W. Barsan, T. Tomsick, L. Sauerbeck, J. Spilker, J. Duldner, J. Khoury, Early hemorrhage growth in patients with intracerebral hemorrhage, Stroke 28 (1) (1997) 1–5.
[7] S.M. Davis, J. Broderick, M. Hennerici, N.C. Brun, M.N. Diringer, S.A. Mayer, K. Begtrup, T. Steiner, V.I.I.I.H.T.I. recombinant activated factor, hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage, Neurology 66 (8) (2006) 1175–1181.
[8] S.A. Mayer, N.C. Brun, K. Begtrup, J. Broderick, S. Davis, M.N. Diringer, B.E. Skolnick, T. Steiner, V.I.I.I.H.T.I. recombinant activated factor, recombinant activated factor VII for acute intracerebral hemorrhage, N. Engl. J. Med. 352 (8) (2005) 777–785.
[9] D. Rodriguez-Luna, M. Rubiera, M. Ribo, P. Coscojuela, S. Pineiro, J. Pagola, M. Hernandez-Guillamon, B. Ibarra, F. Romero, J. Alvarez-Sabin, J. Montaner, C.A. Molina, Ultraearly hematoma growth predicts poor outcome after acute intracerebral hemorrhage, Neurology 77 (17) (2011) 1599–1604.
[10] C. Delcourt, Y. Huang, H. Arima, J. Chalmers, S.M. Davis, E.L. Heeley, J. Wang, M.W. Parsons, G. Liu, C.S. Anderson, I. Investigators, Hematoma growth and outcomes in intracerebral hemorrhage: the INTERACT1 study, Neurology 79 (4) (2012) 314–319.
[11] H.B. Brouwers, S.M. Greenberg, Hematoma expansion following acute intracerebral hemorrhage, Cerebrovasc. Dis. 35 (3) (2013) 195–201.
[12] R. Wada, R.I. Aviv, A.J. Fox, D.J. Sahlas, D.J. Gladstone, G. Tomlinson, S.P. Symons, CT angiography "spot sign" predicts hematoma expansion in acute intracerebral hemorrhage, Stroke 38 (4) (2007) 1257–1262.
[13] J.J. Heit, M. Iv, M. Wintermark, Imaging of intracranial hemorrhage, J. Stroke 19 (1) (2017) 11–27.
[14] Q. Li, Q.J. Liu, W.S. Yang, X.C. Wang, L.B. Zhao, X. Xiong, R. Li, D. Cao, D. Zhu, X. Wei, P. Xie, Island sign: an imaging predictor for early hematoma expansion and poor outcome in patients with intracerebral hemorrhage, Stroke 48 (11) (2017) 3019–3025.
[15] Q. Li, G. Zhang, Y.J. Huang, M.X. Dong, F.J. Lv, X. Wei, J.J. Chen, L.J. Zhang, X.Y. Qin, P. Xie, Blend sign on computed tomography: novel and reliable predictor for early hematoma growth in patients with intracerebral hemorrhage, Stroke 46 (8) (2015) 2119–2123.
[16] Q. Li, G. Zhang, X. Xiong, X.C. Wang, W.S. Yang, K.W. Li, X. Wei, P. Xie, Black hole sign: novel imaging marker that predicts hematoma growth in patients with intracerebral hemorrhage, Stroke 47 (7) (2016) 1777–1781.
[17] D. Ng, L. Churilov, P. Mitchell, R. Dowling, B. Yan, The CT swirl sign is associated with hematoma expansion in intracerebral hemorrhage, AJNR Am. J. Neuroradiol. 39 (2) (2018) 232–237.
[18] N.A. Al-Nakshabandi, The swirl sign, Radiology 218 (2) (2001) 433.
[19] L.R. Caplan, Recognizing and preventing intracerebral hematoma expansion, JAMA Neurol. 73 (8) (2016) 914–915.
[20] Q. Li, Y.Q. Shen, X.F. Xie, M.Z. Xue, D. Cao, W.S. Yang, R. Li, L. Deng, M. Wei, F.J. Lv, G.F. Wu, Z.P. Tang, P. Xie, Expansion-prone hematoma: defining a population at high risk of hematoma growth and poor outcome, Neurocrit. Care 30 (3) (2019) 601–608.
[21] A. Morotti, H.B. Brouwers, J.M. Romero, M.J. Jessel, A. Vashkevich, K. Schwab, M.R. Afzal, C. Cassarly, S.M. Greenberg, R.H. Martin, A.I. Qureshi, J. Rosand, J.N. Goldstein, Intensive blood pressure reduction and spot sign in intracerebral hemorrhage: a secondary analysis of a randomized clinical trial, JAMA Neurol. 74 (8) (2017) 950–960.
[22] P.B. Sporns, M. Schwake, R. Schmidt, A. Kemmling, J. Minnerup, W. Schwindt,

C. Cnyrim, T. Zoubi, W. Heindel, T. Niederstadt, U. Hanning, Computed tomographic blend sign is associated with computed tomographic angiography spot sign and predicts secondary neurological deterioration after intracerebral hemorrhage, Stroke 48 (1) (2017) 131–135.
[23] A. Morotti, G. Boulouis, A. Charidimou, K. Schwab, C. Kourkoulis, C.D. Anderson, M.E. Gurol, A. Viswanathan, J.M. Romero, S.M. Greenberg, J. Rosand, J.N. Goldstein, Integration of computed tomographic angiography spot sign and noncontrast computed tomographic hypodensities to predict hematoma expansion, Stroke 49 (9) (2018) 2067–2073.
[24] A. Morotti, J.M. Romero, M.J. Jessel, H.B. Brouwers, R. Gupta, K. Schwab, A. Vashkevich, A. Ayres, C.D. Anderson, M.E. Gurol, A. Viswanathan, S.M. Greenberg, J. Rosand, J.N. Goldstein, Effect of CTA tube current on spot sign detection and accuracy for prediction of intracerebral hemorrhage expansion, AJNR Am. J. Neuroradiol. 37 (10) (2016) 1781–1786.
[25] R.U. Kothari, T. Brott, J.P. Broderick, W.G. Barsan, L.R. Sauerbeck, M. Zuccarello, J. Khoury, The ABCs of measuring intracerebral hemorrhage volumes, Stroke 27 (8) (1996) 1304–1305.
[26] E.F. Chang, M. Meeker, M.C. Holland, Acute traumatic intraparenchymal hemorrhage: risk factors for progression in the early post-injury period, Neurosurgery 58 (4) (2006) 647–656 discussion 647-56.
[27] J.P. Broderick, T.G. Brott, J.E. Duldner, T. Tomsick, G. Huster, Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality, Stroke 24 (7) (1993) 987–993.
[28] P.S. Bhattathiri, B. Gregson, K.S. Prasad, A.D. Mendelow, S. Investigators, Intraventricular hemorrhage and hydrocephalus after spontaneous intracerebral hemorrhage: results from the STICH trial, Acta Neurochir. Suppl. 96 (2006) 65–68.
[29] S. Sato, H. Arima, Y. Hirakawa, E. Heeley, C. Delcourt, R. Beer, Y. Li, J. Zhang, E. Juettler, J. Wang, P.M. Lavados, T. Robinson, R.I. Lindley, J. Chalmers, C.S. Anderson, I. Investigators, The speed of ultraearly hematoma growth in acute intracerebral hemorrhage, Neurology 83 (24) (2014) 2232–2238.
[30] S.A. Mayer, Ultra-early hemostatic therapy for intracerebral hemorrhage, Stroke 34 (1) (2003) 224–229.
[31] S.A. Mayer, A. Lignelli, M.E. Fink, D.B. Kessler, C.E. Thomas, R. Swarup, R.L. Van Heertum, Perilesional blood flow and edema formation in acute intracerebral hemorrhage: a SPECT study, Stroke 29 (9) (1998) 1791–1798.
[32] H. Takahashi, T. Urano, N. Nagai, Y. Takada, A. Takada, Progressive expansion of hypertensive intracerebral hemorrhage by coagulopathy, Am. J. Hematol. 59 (2) (1998) 110–114.
[33] X. Xu, J. Zhang, K. Yang, Q. Wang, B. Xu, X. Chen, Accuracy of spot sign in predicting hematoma expansion and clinical outcome: a meta-analysis, Medicine 97 (34) (2018) e11945.