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Comparison of Swirl Sign and Black Hole Sign in Predicting Early Hematoma Growth in Patients with Spontaneous Intracerebral Hemorrhage

Background

Spontaneous intracerebral hemorrhage (ICH) is an acute neurological emergency associated with high morbidity and mortality [1,2]. It is estimated to account for approximately 10% to 20% of all strokes [3]. Early hematoma growth, which occurs in 1/3 of patients when scanned within 6 h, is one of the most important determinants of mortality and functional outcome [4,5]. The restricting early hematoma growth may be useful [6]. The computed tomographic angiography (CTA) spot sign (and derived spot sign score) is a reliable sign for predication of early hematoma growth, early mortality, and poor outcome [7,8]. However, early CTA examination is not available in all clinical settings. In addition, several renal function impairment and allergic reactions to contrast medium restrict the CTA examination.

In recent years, noncontrast computed tomography (NCCT) imaging markers, such as blend sign [9], black hole sign (BHS) [10], and hypodensities [11], have been identified as promising imaging markers for predicting early hematoma growth. The swirl sign (SS), which was originally described as areas of low attenuation or radiolucency within hyperattenuated hematomas, indicates active bleeding in epidural hematoma patient [12]. In a study of 203 patients with acute ICH, Selariu et al. documented that SS is an independent predictor of death at 1 month and functional outcome at 3 months [13]. However, the ability of swirl sign to predict early hematoma growth remains controversial. In 2016, Li et al. first proposed using the black hole sign to predict early hematoma growth [10]. More recently, Yu et al. validated the predictive value of BHS in predicting early hematoma growth [14], but the predictive values of BHS and SS in predicting early hematoma growth have never been compared. Therefore, we performed the present study to investigate the role of BHS and SS in predicting early hematoma growth.

Material and Methods

Patients

We analyzed patients with spontaneous ICH aged >18 years who were admitted to our hospital between July 2011 and October 2015 from our prospective ongoing database. The inclusion criteria of this study were as follows: (1) ICH was confirmed on NCCT scan within 6 h after onset of symptoms; (2) the follow-up CT scan was obtained within 24 h after the initial CT scan. The exclusion criteria were as follows: (1) patients suffered from brain tumor, head trauma, or arteriovenous malformation, rupture of an intracranial aneurysm, hemorrhagic infarction, or primary intraventricular hemorrhage; (2) anticoagulation-associated bleeding; (3) surgical evacuation of hematoma before the follow- up CT scan. The demographical data, previous medical history, cigarette smoking, alcohol consumption, medication history, Glasgow coma scale, and blood pressure were recorded. This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. Written informed consult was obtained from all participants or their relatives.

Imaging analysis

The initial and follow-up CT scans were performed using standard clinical parameters with axial 5-mm section thickness. The images were obtained and stored for further evaluation. Hematoma was assessed and classified as lobar, deep, and infratentorial. According to previous definition, the swirl sign on the NCCT was defined as follows: (1) a hypo- or iso-attenuation region (compared to the attenuation of brain parenchyma) within the hyperattenuation hematoma; (2) shape may be rounded, streak-like, or irregular [13]. The black hole sign on the NCCT was defined as follows: (1) a hypoattenuation area (black hole) encapsulated within the hyperattenuation hematoma; (2) the black hole could be round, oval, or rodlike, but was not connected to the adjacent brain tissue; (3) the black hole should have a clear border; (4) the hematoma should have at least a 28 Hounsfield unit (HU) difference between the 2 density regions [10].Two experienced readers who were blinded to all clinical data and follow-up CT images independently evaluated the presence of SS and BHS on initial CT images in all patients. Discrepancies in judging the occurrence of SS and BHS were settled by joint discussion of the 2 readers. Early hematoma growth was defined as an increase of hematoma volume >33% or absolute hematoma growth >6 mL from initial CT scan [15]. The hematoma volume was measured by abc/2 formula [16]. Illustrative SS and BHS on initial CT images and follow-up images are shown in Figure 1.

Statistical analysis

All statistical analyses were performed with commercially available software, SPSS version 19.0 (SPSS, Inc). Continuous variables are expressed as mean (SD) values or median (interquartile range [IQR]) values, as appropriate, and discrete variables are expressed as counts (percentages). Statistical significance was determined by the χ^2 test, the Fisher exact test, the *t* test, Z test, and the Mann-Whitney test, as appropriate. Data with a P value of less than 0.05 were considered significant. Multivariate logistic regression models were used to investigate factors that were independently associated with early hematoma growth. Inter-rater reliability of SS and BHS were estimated by κ values.

Figure 1. Illustration of swirl sign, black hole sign, and follow-up CT images. (**A**) A 60-year-old man presented with sudden onset of left-sided paralysis. Admission CT image performed 1 h after onset of symptoms showing thalamic ICH with a swirl sign (arrow) and the hematoma volume was 16.57 ml. (**B**) Hematoma volume remains the same on follow-up CT scan performed 23 h after onset of symptoms. (**C**) A 75-year-old man with left deep ICH. Initial CT image performed 2 h after onset of symptoms shows black hole sign (arrow). (**D**) Follow-up CT image 4 h later shows significant hematoma growth.

Results

A total of 200 patients (135 men and 65 women) with spontaneous ICH fulfilled the inclusion criteria and were enrolled in our study. The mean age of the patients was 60.5±12.4 years (age range, 27–90 years). The hematoma was located deep in 80%, in cerebral lobes in 13%, and infratentorial in 7%. Hematoma growth was observed in 71 patients (35.5%) with ICH. There were no statistically significant differences in age, sex, hypertension, diabetes mellitus, smoking, alcohol drinking, and intraventricular hemorrhage. The mean baseline hematoma volume was 18.5 ml (interquartile range, 10.3–35.4 ml) in patients

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Table 1. Baseline characteristics between patients with and without hematoma growth.

CT – computed tomography; GCS – Glasgow Coma Scale; IVH – intraventricular hemorrhage; IQR – inter-quartile range; SD – standard deviation.

with early hematoma growth when compared with 11.7 ml (interquartile range, 6.7–16.6 ml) in patients without early hematoma growth (P<0.001). The onset-to-imaging time in patients with early hematoma growth was shorter than that in patients without early hematoma growth (P<0.001). The mean baseline Glasgow coma scale score in patients with early hematoma growth was 12 (interquartile range, 8–14), while that in patients without early hematoma growth was 14 (interquartile range, 12–15) (P<0.001). Detailed data comparing patients with and without early hematoma growth are displayed in Table 1.

BHS was found in 30 (15%) of 200 patients with ICH, and SS was found in 70 (35%) of 200 patients with ICH at initial CT. Of the 71 patients with early hematoma growth, BHS was found on initial CT scans in 24 (33.8%) and the SS in 33 (46.5%). Detailed baseline demographic, as well as clinical and radiological characteristics, between patient BHS and SS are displayed in Table 2. The inter-rater agreement for identifying BHS and SS were 0.939 and 0.816, respectively, between the 2 readers. The sensitivity, specificity, and positive and negative predictive value of BHS for predicting early hematoma growth were 33.8%, 95.3%, 80.0%, and 72.0%, respectively. The sensitivity, specificity, and positive and negative predictive value of SS for predicting early hematoma growth were 46.5%, 71.3%, 47.0%, and 71%, respectively. The receiver operating characteristic (ROC) of the 2 signs for the prediction of early hematoma growth are shown in Figure 2. The area under the curve (AUC) was 0.646 for BHS and 0.589 for SS (P=0.08).

In univariate logistic regression, admission Glasgow coma scale, higher baseline hematoma volume, time to CT, and presence of BHS and SS on initial CT scan were associated with early hematoma growth (Table 3). In multivariate logistic regression, the presence of BHS on initial CT remained independently

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Table 2. Baseline characteristics of patients with black hole sign positive and swirl sign positive.

Variables		Black hole sign positive (n=30)		Swirl sign positive (n=70)	
Demographic					
Mean age, y (SD)	62.5	(13.0)	61.1	(11.7)	
Sex, male, n (%)	20	(66.7)	46	(65.7)	
Medical history					
Alcohol consumption, n (%)	16	(53.3)	31	(44.3)	
Smoking, n (%)	16	(53.3)	32	(45.7)	
Hypertension, n (%)	20	(66.7)	53	(75.7)	
Diabetes mellitus, n (%)	3	(10)	8	(11.4)	
Clinical features					
Systolic blood pressure, mmHg (SD)	164.7	(27.6)	167.1	(26.1)	
Diastolic blood pressure, mmHg SD)	96.7	(14.5)	94.5	(14.2)	
Baseline hematoma volume, ml(IQR)	24.3	$(14.9 - 50.8)$	18.4	$(13.4 - 29.0)$	
Onset-to-imaging time, h(IQR)	2	$(1 - 3.25)$	$\overline{2}$	$(1-4)$	
Baseline GCS score, median(IQR)	10	$(7-14)$	12	$(8-14)$	
IVH at initial CT, n (%)	11	(36.7)	31	(44.3)	
Lobar hemorrhage, n (%)	8	(26.7)	11	(15.7)	
Deep hemorrhage, n (%)	21	(70)	58	(82.9)	
Infratentorial hemorrhage, n (%)	$\mathbf{1}$	(3.3)	$\mathbf{1}$	(1.4)	

CT – computed tomography; GCS – Glasgow Coma Scale; IVH – intraventricular hemorrhage; IQR – inter-quartile range; SD – standard deviation.

Figure 2. Receiver-operating characteristic (ROC) curve using a binary definition of early hematoma growth. The AUC value of the black hole sign=0.646 and the AUC value of the swirl sign=0.589; P=0.08.

associated with early hematoma growth (odds ratio, 8.51 [95%CI, 2.55–28.40]; P <0.001). However, SS did not predict early hematoma growth in the multivariate logistic analysis (odds ratio, 0.61 [95%CI, 0.26–1.48]; P=0.276; Table 4).

Discussion

In this study, we found that BHS is more accurate than SS in prediction of early hematoma growth when comparing the 2 signs in primary ICH patients. The AUC value of the BHS was 0.646, which was higher than that of SS (P=0.08). Controversy exists over whether SS is an independent predictor of early hematoma growth. In a study of 203 patients with ICH, Selariu et al. first defined SS as an imaging marker for predicting early hematoma growth; the swirl sign was observed in 30% (61/203) of ICH patients in their study. However, the ability to predict early hematoma growth was not investigated [13]. In a study of 56 patients with ICH, Kim et al. found SS was observed in 13 of 56 (23%) patients with ICH, and SS was not

Table 3. Univariate analyses for early hematoma growth.

CT – computed tomography; GCS – Glasgow Coma Scale; IVH – intraventricular hemorrhage; IQR – inter-quartile range; SD – standard deviation. * Per unit change in regressor.

Table 4. Multivariate analysis for early hematoma growth.

GCS – Glasgow Coma Scale. * Per unit change in regressor.

independently predictive of hematoma growth [17]. In another study, Gökçe et al. reported that SS was observed in 36 of 45 (80%) patients with ICH [18]. Interestingly, 46.6% (21/45) of patients had anticoagulant-associated ICH, and the time of flow-up CT varied from 1.5 to 192 h, but they did not define hematoma growth. In a retrospective study, Connor et al. studied 71 ICH patients presenting <24 h after onset of symptoms with baseline NCCT, and 24-h follow-up CT [19]. Their study showed SS was observed in 46% (33/71) of patients. Multivariate analysis demonstrated SS is independently associated with early hematoma growth. Recently, Boulouis et al. [11] reported that 207 of 1029 (20%) ICH patients had SS. In univariate analysis, SS was associated with early hematoma growth, but in the multivariable model, SS cannot independently predict hematoma growth. Strikingly, SS was reported in 20% to 80% of patients with ICH. In our study, SS was observed in 35% of patients with ICH. SS can predict early hematoma growth in univariate analysis, but after multivariate analysis, SS could not predict early hematoma growth, which is in accordance with most previous studies. In contrast, BHS, as proposed by Li et al. [10], is a novel NCCT for early hematoma growth in primary ICH, with a high inter-rater agreement (0.939). This could be explained by the rigorous definition of BHS.

BHS and SS are both imaging markers that reflect hemorrhage density heterogeneity. Hematoma growth may occur in a cascaded pattern, with initial bleeding causing secondary peripheral vessels rupture for ongoing bleeding [20,21]. The CT attenuation of blood is dependent on the time course of the bleeding [22], so the heterogeneity of the hematoma represents blood of different ages. In addition, the hypoattenuation area may indicate the fresh liquid blood bleeding [23]. However, the hypoattenuation region that connects to adjacent brain tissue may be a normal brain parenchyma, which may

be judged as SS according to Selariu's definition [13], and this might limit the ability to predict early hematoma growth. SS has a vague definition, and the evaluation of SS is more subjective. In BHS, a clear border and a delta of \geq 28 HU between the 2 density regions can improve the reliability and subjectivity. Therefore, the inter-rater reliability is higher than with SS. The rigorous definition of BHS results in a high specificity of BHS (95.3%) but a low sensitivity (33.8%).

Many studies have documented that the CTA spot sign is a good predictor of early hematoma growth [24]. Recent studies have assessed the correction between CTA spot sign and NCCT markers. In a study of 115 patients with ICH, Zheng et al. reported that blend sign and CTA spot sign are good predictors for early hematoma growth [25]. In a study of 129 patients with ICH, Yu et al. demonstrated that the presence of the BHS is associated with the spot sign, and BHS and CTA spot sign are both predictors of early hematoma growth [14]. Interestingly, they also found early hematoma growth can occur in BHS-positive but CTA spot sign-negative patients.

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There are several limitations to the present study. Some NCCT appearances can also predict early hematoma growth, but we only compared SS and BHS because SS and BHS are more comparable. This was a single-center study, and multicenter studies are needed to further valuate the predictive value.

Conclusions

To the best of our knowledge, there is no previous study comparing SS and BHS in the prediction of early hematoma growth. Our study shows that BHS is be good predictor of hematoma growth, but baseline NCCT swirl sign does not independently predict hematoma growth in patients with ICH.

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Conflict of interest

None.

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