Original Article

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A reliable grading system for prediction of hematoma expansion in intracerebral hemorrhage in the basal ganglia

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Summary **Hematoma expansion (HE) is an independent predictor of poor outcome and secondary neurological deterioration in intracerebral hemorrhage (ICH) and is associated with high morbidity and mortality. Noncontrast computed tomography (NCCT) may identify the sites of active extravasation. Therefore, we have attempted to (1) devise a reliable and easy-to-use prediction score to predict the risk of HE in ICH and (2) validate the accuracy of this grading system and perform an independent analysis of HE predictors. We included patients in whom an intracerebral hemorrhage (ICH) occurred in the basal ganglia between Jan. 2015 and Jan. 2018. These patients had undergone a baseline CT scan at Qinghai Provincial People's Hospital within 24 hours after the onset of ICH symptoms. Two observers independently assessed the presence of the island sign, blend sign, or swirl sign on an NCCT scan during patient selection. Patients underwent a baseline NCCT scan and 24-hour NCCT follow-up for analysis of HE. The accuracy of this grading system was assessed. Independent predictors of HE were identified using multivariable regression. Of 266 patients with ICH, 61 (22.93%) presented with the island sign, 63 (23.68%) presented with the blend sign, and 50 (18.80%) presented with the swirl sign. The overall incidence of HE was 37.22% (99/266). Of 125 patients (46.99%) who underwent a baseline CT scan within 6 hours of onset, 141 (53.01%) underwent a scan in 6-24 hours. Multivariable logistic regression analysis identified the hematoma volume (OR, 0.974; $P = 0.042$), intraventricular hemorrhage (IVH) extension (OR, 3.225; $P = 0.003$), time from onset to the baseline CT scan (OR, 0.986; $P < 0.001$), and anticoagulant use or an international normalized ratio (INR) > 1.5 (OR, 3.362; $P = 0.006$) as closely associated with HE. In conclusion, the grading system demonstrated reliable accuracy at predicting HE. The grading system demonstrated acceptable accuracy in an independent single-institution study. The role of the grading system in predicting HE and poor outcome in patients with ICH is significant. NCCT imaging markers may serve as key markers for HE prediction.**

Keywords: Hematoma expansion, intracerebral hemorrhage, noncontrast computed tomography, grading system, basal ganglia

1. Introduction

Intracerebral hemorrhage (ICH) is a common disorder of the cerebral small vessels. ICH is a dynamic disorder, with up to 1/3 of patients suffering continued bleeding after initial onset (*1*). ICH accounts for about 10% to 30% of all strokes worldwide (*2*) and it has a poor prognosis with a morbidity and mortality approaching 50% at 30 days (*3*).

The mechanism of hematoma expansion (HE) in ICH is not clear at this time, and a reliable grading system is needed to assess HE. The lack of an accurate grading system could lead to inconsistencies in the assessment of HE and poor functional prognosis and preclude comparisons of the effectiveness of treatment at different institutions.

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The purpose of this study was to devise a reliable score for prediction of HE in ICH based on several objective predictors that can be ascertained soon after onset. To that end, the current study devised such a grading system to assess the risk of HE, thus paving the way forward for standardization of HE treatment in ICH.

2. Materials and Methods

2.1. *Patient selection*

The Ethics Committee of Qinghai Provincial People's Hospital approved this retrospective study. Subjects were patients (> 18 years) with ICH between Jan. 2015 and Jan. 2018 who had undergone a baseline CT scan at this Hospital within 24 hours after the onset of ICH symptoms. A follow-up NCCT scan was performed within 24 hours after the baseline CT scan. At the baseline, all hematomas were located in the basal ganglia. Patients who had undergone urgent hematoma evacuation before the follow-up CT scan were excluded from this study. Also excluded were patients whose ICH was secondary to vessel malformation, head trauma, cerebral aneurysm, brain tumor, or brain infarction. The time to initial and follow-up CT scans and fundamental clinical variables were recorded for each patient. Patients with large fluctuations in blood pressure during hospitalization had their blood pressure continuously monitored while receiving standard treatment for hypertension.

All of the patients with HE were diagnosed using NCCT. The rate of HE can truly reflect basic pathological changes, so an attempt was made to devise a grading system to evaluate the risk of HE in ICH.

2.2. *Imaging analysis*

CT images can be analyzed in two ways: (1) imaging findings based on changes in hematoma density and shape on CT; and (2) initial hematoma volume and follow-up hematoma volume.

HE in ICH is identified based on the baseline CT scan after onset and a follow-up CT scan within 24 hours. All of the current patients were classified into 3 categories based on hematoma imaging, including changes in density and shape on CT: the island sign, blend sign, or swirl sign.

The island sign was defined as (*i*) ≥ 3 scattered small hematomas entirely separate from the main hematoma; (*ii*) or ≥ 4 small hematomas partly or all of which may connect to the main hematoma; (*iii*) The scattered small hematomas were round or oval and were separate from the main hematoma; (*iv*) The small hematomas that connected to the main hematoma were bubble-like or bud-like but not segmented (*4*).

The blend sign is defined as blending of a relatively hypoattenuated area with an adjacent hyperattenuated region within the hematoma with a well-defined margin between these regions and a delta of at least 18 Hounsfield units between the 2 regions (*5*).

The swirl sign was defined as: hypo- or iso-density within a region of a hyperdensity that correlates with active hemorrhage on surgical evacuation (*6*).

HE in ICH is defined as a 33% increase in hematoma volume or > 6 mL at the time of the follow-up CT scan according to previous studies (*7,8*).

Two experienced observers (including an imaging physician and a neurosurgeon) who were blinded to the clinical information on patients reviewed all images to identify the 3 imaging markers. Discrepancies regarding the presence of the markers were resolved through consensus. 3D Slicer (Version 4.8.0, Harvard University, NY) was used to calculate the hematoma volume.

2.3. *Statistical analysis*

All statistical analyses were performed using the software package SPSS (Version 19.0; IBM Corporation, Armonk, NY). Medians and interquartile ranges (IQRs) or the mean ± standard deviation (SD) was used to describe continuous variables, and percentage (%) was used to describe discrete variables.

The rate of HE was assessed using the t test or χ^2 test. Univariate and multivariate logistic regression analyses were used to assess predictors associated with HE. The same patient data were used to identify the accuracy of the HE prediction scores. $P < 0.05$ was considered statistically significant.

3. Results

3.1. *Baseline characteristics*

The characteristics of the study population are shown in Table 1. Subjects included 173 men (65.04%) and 93 women (34.96%) with a mean age of 58.98 ± 10.91 years. In the 266 patients, the hematoma was located in the basal ganglia at the baseline, including 99 (37.22%) with HE and 167 (62.78%) with non-HE. The time from onset to the initial CT scan was within 6 hours in 125 patients (46.99%) and 6-24 hours in 141 (53.01%). The overall median initial hematoma volume was 14.93 mL (IQR, 7.49-24.32 mL). Intraventricular hemorrhage (IVH) extension was noted in 83 of 266 patients (31.20%) on the baseline CT scan. Of 266 patients, 44 (16.54%) were using an anticoagulant or had an international normalized ratio (INR) > 1.5. The overall incidence of HE was 37.22% (99 of 266).

3.2. *Frequency and characteristics of imaging markers*

Of 1,400 potential subjects, 266 served as subjects

for analysis of HE. The island sign was noted in 48 (48.48%) of 99 patients with HE versus 13 (7.78%) of 167 patients without HE on a CT scan during patient selection. The blend sign was noted in 34 (34.34%) of 99 patients versus 29 (17.37%) of 167 patients without HE. The swirl sign was noted in 25 (25.25%) of 99 patients versus 25 (14.97%) of 167 patients without HE. The original clinical and imaging characteristics of patients with and without CT markers are shown in Table 2.

Table 1. Baseline demographic, clinical and imaging characteristics of the population in this study

Items	Patients with HE (*n* = 99)	Patients without HE (*n* = 167)	*P*
Demographic characteristics			
Mean age, y (SD)	59.61 ± 10.36	58.35 ± 11.46	0.373
Sex, male, *n* (%)	56 (56.57)	117 (70.06)	0.725
Clinical features			
Time to baseline CT scan, Median (IQR), h	5 (4-8)	6 (5-8)	0.019
Baseline hematoma volume (IQR), mL	16.34 (8.40-29.31)	14.84 (6.98-22.63)	0.108
IVH extension at initial CT, *n* (%)	46 (46.46)	37 (22.16)	< 0.001
Anticoagulant use or an INR > 1.5, *n* (%)	27 (27.27)	17 (10.18)	< 0.001
Presence of SAH, *n* (%)	7 (7.07)	11 (6.59)	0.879
Presence of MLS, *n* (%)	18 (18.18)	26 (15.57)	0.579
Imaging markers			
Island sign, *n* (%)	48 (48.48)	13 (7.78)	< 0.001
Blend sign, *n* (%)	34 (34.34)	29 (17.37)	< 0.001
Swirl sign, *n* (%)	25 (25.25)	25 (14.97)	0.038

HE, hematoma expansion; CT, computed tomography; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; SD, standard deviation; IQR, inter-quartile range; INR, international normalized ratio.

Table 2. Comparison of baseline demographic, clinical, and imaging characteristics between patients with and without CT imaging markers

Items	IS (+), *n* = 61	IS (–), *n* = 205	*P*
Demographic characteristics			
Mean age, y (SD)	57.92 ± 9.50	59.09 ± 11.49	0.469
Sex, male, *n* (%)	46 (75.41)	127 (61.95)	0.053
Clinical features			
Baseline ICH volume (IQR), mL	24.70 (8.49-29.00)	14.51 (7.28-22.33)	< 0.01
Anticoagulant use or an INR > 1.5, *n* (%)	13 (29.55)	31 (70.45)	0.253
Time to baseline CT scan, median (IQR), h	5 (4-8)	6 (4-8)	0.298
IVH extension, *n* (%)	25 (39.68)	58 (28.29)	0.975
HE, *n* (%)	48 (78.69)	51 (24.88)	< 0.001
Items	BS (+), *n* = 63	BS (–), *n* = 203	*P*
Demographic characteristics			
Mean age, y (SD)	57.30 ± 11.54	59.29 ± 10.89	0.213
Sex, male, *n* (%)	45 (71.43)	128 (63.05)	0.223
Clinical features			
Baseline ICH volume (IQR), mL	20.78 (13.95-32.96)	12.21 (6.00-22.03)	< 0.01
Anticoagulant use or an INR > 1.5, *n* (%)	13 (29.55)	31 (70.45)	0.317
Time to baseline CT scan, median (IQR), h	6 (4-9)	5 (4-8)	0.212
IVH extension, *n* (%)	20 (31.75)	63 (31.03)	0.915
HE, *n* (%)	34 (53.97)	65 (32.02)	0.002
Items	SS (+), *n* = 50	SS (–), *n* = 216	*P*
Demographic characteristics			
Mean age, y (SD)	59.40 ± 10.20	58.69 ± 11.24	0.681
Sex, male, *n* (%)	31 (62.00)	142 (65.74)	0.617
Clinical features			
Baseline ICH volume (IQR), mL	19.89 (11.82-28.28)	14.23 (7.12-22.79)	0.017
Anticoagulant use or an INR > 1.5, *n* (%)	9 (20.45)	35 (79.55)	0.758
Time to baseline CT scan, median (IQR), h	5 (3-7)	6 (4-8)	0.024
IVH extension, *n* (%)	15 (30.00)	68 (31.48)	0.839
HE, *n* (%)	25 (50.00)	74 (34.26)	0.038

IS, island sign; BS, blend sign; SS, swirl sign.

The presence of imaging markers was associated with a larger initial hematoma volume, the island sign (24.70 mL: 14.51 mL; $P < 0.01$), the blend sign (20.78 mL: 12.21 mL; $P < 0.01$), and the swirl sign (19.89 mL: 14.23 mL; $P = 0.017$). Anticoagulant use or an INR > 1.5, the time from onset to the baseline CT scan on admission, and IVH extension did not differ significantly in patients with or without imaging markers.

The 2 observers identified imaging markers with a high level of inter-observer agreement ($\kappa = 0.90$). The island sign predicted HE with a sensitivity of 48.48%, a specificity of 92.22%, a positive predictive value of 78.69%, and a negative predictive value of 75.12%. The blend sign predicted HE with a sensitivity of 34.34%, a specificity of 82.63%, a positive predictive value of 53.97%, and a negative predictive value of 67.98%. The swirl sign predicted HE with a sensitivity of 25.25%, a specificity of 85.03%, a positive predictive value of 50.00%, and a negative predictive value of 65.74%. All of the imaging markers studied had satisfactory ability to predict HE. These markers differed significantly in the sensitivity, specificity, and NPV with which they predicted HE (all $P < 0.05$). The island sign had better ability to predict HE. Relevant data are shown in Table 3.

Univariate and multivariate logistic regression analysis were performed to assess the association between various clinical and imaging parameters and HE, as shown in Table 4. Univariate analysis indicated that the time to the baseline CT scan (odds ratio (OR), 1.064; 95% confidence interval (CI), 1.003-1.127; $P = 0.038$), initial ICH volume (OR, 1.021; 95% CI, 1.003-1.038; $P = 0.018$), IVH extension (OR, 3.049; 95% CI, 1.781-5.222; $P < 0.001$), anticoagulant use or an INR > 1.5 (OR, 3.309; 95% CI, 1.695-6.458; $P < 0.001$), and the presence of imaging markers (island sign, blend sign, or swirl sign) on a CT scan upon admission (all $P < 0.005$) were associated with HE. Multivariate logistic regression analysis indicated that the time to the baseline CT scan (OR, 0.986; 95% CI, 0.926-1.014; $P < 0.001$), the baseline ICH volume (OR, 0.974; 95% CI, 0.949-0.999; $P = 0.042$), anticoagulant use or an INR > 1.5 (OR, 3.362; 95% CI, 1.415-7.988; $P = 0.006$), and the presence of imaging markers on the baseline CT scan ($P < 0.001$ for all) independently predicted HE. The results of logistic regression analysis for HE are shown in Table 4.

3.3. *Devising and validation of the grading system*

A grading system was devised using the parameters from multivariable regression in Table 4, including imaging markers (island sign, blend sign, or swirl sign), the time from onset to the initial CT scan, anticoagulant

Table 3. Sensitivity, specificity, PPV, and NPV of CT imaging markers

Items	Island sign (95% CI)	Blend sign (95% CI)	Swirl sign (95% CI)	*P*
Sensitivity	48.48 (42.48-54.49)	34.34 (28.64-40.05)	25.25 (20.03-30.47)	0.028
Specificity	92.22 (89.00-95.44)	82.63 (78.08-87.19)	85.03 (80.74-89.32)	0.003
PPV	78.69 (73.77-83.61)	53.97 (47.98-59.96)	50.00 (43.99-56.01)	0.094
NPV	75.12 (69.93-80.32)	67.98 (62.37-73.59)	65.74 (60.04-71.44)	0.003

PPV, positive predictive value; NPV, negative predictive value.

Table 4. Univariate and multivariate analysis of predictors for HE

Items	OR	95% CI	*P*
Univariate analysis			
Age	1.010	0.998-1.033	0.372
Time to baseline CT scan	1.064	1.003-1.127	0.038
Baseline ICH volume	1.021	1.003-1.038	0.018
IVH extension	3.049	1.781-5.222	< 0.001
Anticoagulant use or an INR > 1.5	3.309	1.695-6.458	< 0.001
Presence of imaging markers			
Island sign	11.149	5.593-22.224	< 0.001
Blend sign	2.489	1.399-4.430	0.003
Swirl sign	1.919	1.031-3.573	0.042
Multivariate analysis			
Time to baseline CT scan	0.986	0.926-1.014	< 0.001
Baseline ICH volume	0.974	0.949-0.999	0.042
Anticoagulant use or an INR > 1.5	3.362	1.415-7.988	0.006
IVH extension	3.225	1.501-6.929	0.003
Presence of imaging markers			
Island sign	39.503	15.022-103.882	< 0.001
Blend sign	15.300	5.933-39.456	< 0.001
Swirl sign	9.798	3.785-25.368	< 0.001

CI, confidence interval; OR, odds ratio.

Table 5. Summary of the HE Prediction Grading System

Component	Points
Hours from onset to CT (h)	1
≤ 6	0
6-24	
Baseline ICH volume (mL)	1
≥ 30	0
< 30	
Island sign	1
Present	0
Absent	
Blend sign	1
Present	0
Absent	
Swirl sign	1
Present	0
Absent	
Anticoagulant use or an INR > 1.5	1
Present	0
Absent	
IVH extension	1
Present	0
Absent	

Total points:0-7.

use or an INR > 1.5, and IVH extension. The grading system is shown in Table 5. These factors were used to create a statistical model to predict HE.

Based on the results of the regression model, CT imaging markers (island sign, blend sign, or swirl sign), anticoagulant use or an INR > 1.5, and time from onset to the initial CT scan were the strongest predictors of HE. The results of these regression models have laid the foundation for scoring the prediction of HE in ICH.

Therefore, the score to predict HE in ICH consists of 5 components: changes in density and shape on CT (imaging markers), the time from onset to the initial CT scan, anticoagulant use or an INR > 1.5, baseline ICH volume, and IVH extension. The time from onset to the initial CT scan was further subdivided (≤ 6 h and 6-24 h), as was the baseline ICH volume (≥ 30 mL and < 30 mL). A baseline ICH volume ≥ 30 mL had a sensitivity of 32.32% and a specificity of 80.84%. Each variable was given a specific cutoff based on its relevance to HE. A baseline CT scan performed within 6 hours of onset is critical because it represents the critical nature of HE. The grading system score ranges from 0 to 7 points.

The grading system was used to score patients in order to determine its ability to predict HE, and those results are shown in Table 6. The incidence of HE increased as the score increased. A higher score on the grading system indicated a greater probability of HE ($P < 0.001$). The probability of HE was 3.45% for a score of 0 (1/29), 18.31% (13/71) for a score of 1, 32.53% (27/83) for a score of 2, 61.22% (30/49) for a score of 3, 79.17% (19/24) for a score of 4, and 85.71% (6/7) for a score of. The probability of HE was 100% (3/3) with a score ≥ 6. No patients had a score of 7. The grading system's performance in predicting HE prediction is shown in Table 6.

Table 6. Risk of HE according to the Prediction Grading System

Total Score	Estimate of HE risk, % (*n*)
0	3.45 (1/29)
1	18.31 (13/71)
2	32.53 (27/83)
3	61.22 (30/49)
4	79.17 (19/24)
5	85.71 (6/7)
≥ 6	100 (3/3)

3.4. *Representative case*

A 56-year-old man with hypertension and diabetes mellitus was first admitted to this Hospital for weakness in his right extremities secondary to a left basal ganglia hematoma within 4 hours of the onset of symptoms. A baseline CT scan revealed a combined left basal ganglia hematoma. Two experienced observers (including an imaging physician and a neurosurgeon) who were blinded to the clinical information on the patient reviewed the CT images, and both noted the blend sign and the swirl sign (Figure 1, A). 3D Slicer was used to calculate the baseline ICH volume, which was about 73.29 mL. The patient had been prescribed warfarin for atrial fibrillation. His blood pressure upon admission was 232/103 mmHg, and his Glasgow Coma Scale (GCS) score was 5. His INR upon admission was 1.8. According to the grading system, the patient's score was 5 points (hours from onset to CT = 4; baseline ICH volume = 73.29 mL; presence of the blend sign and swirl sign; and anticoagulant use and INR = 1.8). Accordingly, the patient was deemed to have a high risk of HE. A follow-up NCCT scan was performed 18 hours after onset. 3D-Slicer was again used to measure hematoma volume, which was about 84.50 mL (Figure 1, B).

4. Discussion

Although HE is a common phenomenon in ICH, there is no widely accepted grading system that can be used to predict HE in patients with ICH and to guide clinical treatment and research. A lack of HE prediction scores has presumably lead to large differences in the clinical data collected in clinical studies of ICH and inconsistent treatment strategies. A new grading system has been devised to predict the risk of HE in patients with ICH by analyzing clinical data on patients with ICH at this Hospital. The significance for each component of this grading system is worth discussing. The predictive grading system has five components: the time from onset to the initial CT scan, baseline ICH volume, the presence of imaging markers (island sign, blend sign, or

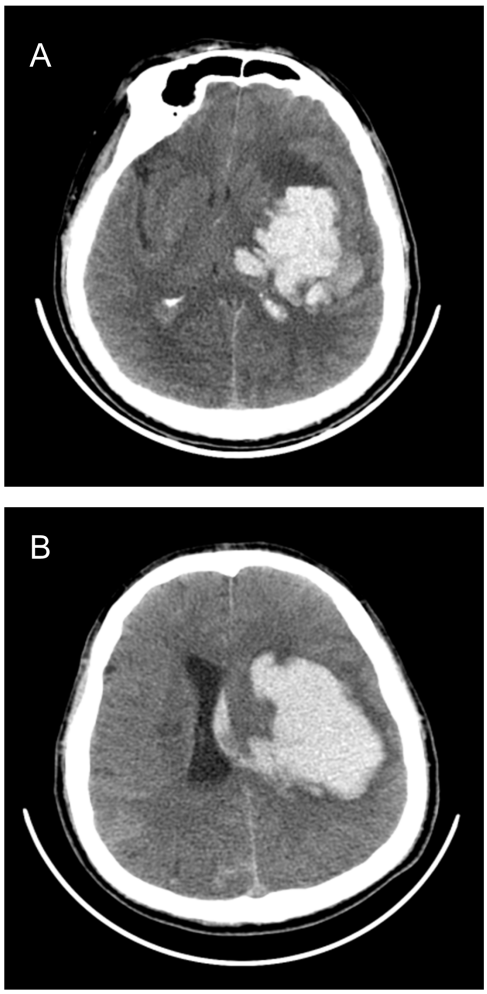

Figure 1. A CT scan showing a combined left basal ganglia hematoma (Figure 1, A) when the patient developed motor weakness in his right extremities during initial admission. A CT scan on second admission revealed a larger left basal ganglia hematoma (Figure 1, B).

swirl sign), anticoagulant use or an INR > 1.5, and IVH extension. This system provides an easily performed method of reasonably predicting HE.

Some of the components of the grading system have been previously cited as independent predictors of HE in ICH. The time from onset to the initial CT scan has been identified as a consistent predictor of HE in various studies (*9,10,12-15*). HE occurs soon after the onset of ICH, usually within 3-6 h, in approximately 1/4 to 1/3 of patients (*10*). In the current study, the time from onset to the initial CT scan was within 6 hours in 125 patients (46.99%) and 6-24 hours in 141 (53.01%). In this study, the time to the baseline CT scan was significantly associated with HE ($P < 0.001$).

In patients with ICH, the presence of NCCT imaging markers in the form of the island sign, the blend sign and/or the swirl sign indicates a greater possibility of HE (*4-6*). The presence of imaging markers has been identified as an independent predictor of HE, and these markers have a reliable accuracy at predicting HE (*4-6,23*). Therefore, these markers could be used to predict HE in ICH. In the current study, the sensitivity, specificity, and NPV of these markers differed significantly ($P < 0.05$ for all). The island sign had better ability to predict HE.

A causal link between anticoagulant use and HE seems logical, but relevant studies have yielded inconsistent results (*7,10,13.15-18*). In the current study, anticoagulant use or an INR > 1.5 was significantly associated with HE ($P < 0.001$). IVH extension and anticoagulant use are also associated with HE according to several previous studies (*11-15*). Moreover, these two variables had been identified as significant predictors of HE in previous studies (*4,19,20*). In the current study, these two risk factors were highly associated with HE (both $P < 0.001$). Therefore, they were included in the grading system developed here. A baseline ICH volume larger than 30 mL has been found to be a risk factor for HE according to a couple of studies (*9,11*). The current study yielded similar results (OR, 0.974; $P = 0.042$). Therefore, baseline ICH volume was included as a predictive parameter with a sensitivity of 32.32% and a specificity of 80.84% (ICH volume ≥ 30 mL).

Recently, a study by Li *et al*. (*4*) found that a lower GCS score is one of critical predictors that can influence HE ($P < 0.001$). Because of differences in anatomy and blood supply between basal ganglia and non-basal ganglia, the current study examined ICH in the basal ganglia in order to reduce bias. Moreover, the GCS was not included as a parameter since all of the patients with ICH had a hematoma located in the basal ganglia. In most people, one hemisphere of the brain is dominant (left or right). When the level of consciousness or ability to speak is assessed in patients with ICH, their GCS will inevitably be inaccurate, and this might influence the results of a grading system.

Brouwers *et al*. (*9*) developed a 9-point score to predict HE based on four parameters: the presence of the spot sign, warfarin use, the time to the initial CT (> 6 h or ≤ 6 h), and baseline ICH volume (< 30 mL, 30-60 mL or > 60 mL). In their study, a higher score resulted in better ability to predict HE. In 2015, Wang *et al*. (*21*) refined the 9-point score by including baseline ICH volume (≤ 10 mL,10-20 mL or > 20 mL) and the time to the initial CT (≤ 1 h, 1-2 h, 2-3 h, 3-4 h, 4-5 h and > 5 h). Based on the 9-point score, Wang *et al.* (*19*) proposed a new 24-point score (BRAIN) and they added two novel parameters: IVH extension and recurrent ICH. The scores from that system are similar to those in previous studies. The higher the score, the greater the probability of HE. Although the accuracy of these two system seems comparable to that of the grading system developed here, this new grading system has several additional advantages. Because of the universality of NCCT, the parameters needed to tally a score with this grading system are readily determined in almost any medical facility. More importantly, imaging makers (island sign, blend sign and/or swirl sign) can be readily

identified in clinical settings. That said, the study by Brouwers *et al.* (*9*) included a larger number of patients with ICH >30 mL, suggesting that the two grading systems might be complementary at predicting HE depending on clinical characteristics.

The predictive grading system devised here can provide a reasonable estimation of the risk for HE in patients with ICH, and it could have useful clinical applications. The grading system indicated that a higher score meant a greater probability of HE ($P < 0.001$). The probability of HE was 3.45% (1/29) for a score of 0, 18.31% (13/71) for a score of 1, 32.53% (27/83) for a score of 2, 61.22% (30/49) for a score of 3, 79.17% (19/24) for a score of 4, and 85.71% (6/7) for a score of 5. The probability of HE was 100% (3/3) for a score ≥ 6. This score may help neurosurgeons to decide which patients with ICH will require closer monitoring or surgery. It may also aid in identifying patients who would benefit most from interventions targeting HE in clinical trials (*22*).

The current study had several limitations. First, this study was retrospective in nature and conducted at a single institution with a relatively small sample size, so the current results need to be verified at other medical facilities. Second, a relationship between HE and neurological deterioration or long-termed clinic functional outcomes was not evident, so a scoring threshold could not be defined to predict clinically significant HE. Future prospective studies need to be conducted to define appropriate thresholds to stratify patients with HE a low versus a high risk of clinical deterioration to guide clinical decision-making. Last, the grading system developed here has not been validated in separate internal or external cohorts. This limits the generalizability of the current results to other patients with ICH. Therefore, the grading system developed here should not be used to make final treatment recommendations or to obtain definitive information on the progression of ICH or prognosis at this stage in time. Future plans are to validate the grading system developed here in an external cohort of patients with ICH.

In conclusion, a quick and easy-to-use grading system was developed and internally validated to predict the risk for HE in a cohort of patients with ICH. This predictive grading system could have major clinical applications.

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