



# Potential of Satellite Sign for Prediction of Hematoma Expansion in Small Spontaneous Hematoma within 7 Days' Follow-Up

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## Abstract

**Background** Hematoma expansion (HE) is the most important modifiable predictor that can change the clinical outcome of intracerebral hemorrhage (ICH) patients. The study aimed to investigate the potential of satellite sign for prediction of HE in spontaneous ICH patients who had follow-up non-contrast computed tomography (NCCT) within 7 days after the initial CT scan.

**Methods** We retrospectively reviewed data and NCCT from 142 ICH patients who were treated at our hospital at Bangkok, Thailand. All included patients were treated conservatively, had baseline NCCT within 12 hours after symptom onset, and had follow-up NCCT within 168 hours after baseline NCCT. HE was initially estimated by two radiologists, and then by image analysis software. Association between satellite sign and HE was evaluated.

**Results** HE occurred in 45 patients (31.7%). Patients with HE had significantly higher activated partial thromboplastin time ( $p = 0.001$ ) and baseline hematoma volume ( $p = 0.001$ ). The prevalence of satellite sign was 43.7%, and it was significantly independently associated with HE ( $p = 0.021$ ). The sensitivity, specificity, and accuracy of satellite sign for predicting HE was 57.8, 62.9, and 61.3%, respectively. From image analysis software, the cutoff of greater than 9% relative growth in hematoma volume on follow-up NCCT had the highest association with satellite sign ( $p = 0.024$ ), with a sensitivity of 55%, specificity of 64.6%, and accuracy of 60.5%.

**Conclusion** Satellite sign, a new NCCT predictor, was found to be significantly associated with HE in Thai population. With different context of Thai population, HE was found in smaller baseline hematoma volume. Satellite sign was found more common in lobar hematoma. Further studies to validate satellite sign for predicting HE and to identify an optimal cutoff in Thai population that is correlated with clinical outcomes are warranted.

## Keywords

- ▶ satellite sign
- ▶ prediction
- ▶ hematoma expansion
- ▶ spontaneous intracranial hemorrhage
- ▶ computed tomography

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## Introduction

Intracerebral hemorrhage (ICH) is a common condition that is associated with a mortality rate as high as 40% at 1 month.<sup>1</sup> Hematoma expansion (HE), which occurs in about 30% of spontaneous ICH patients, has been identified as a factor that causes neurological deterioration and poor outcome.<sup>2</sup> In contrast to other predictors, such as age, underlying disease, initial volume of ICH, and location, HE is the most important modifiable predictor that can change the outcome of ICH.<sup>3</sup> Several previous studies found and reported the spot sign on computed tomography angiography (CTA) to be a good predictor of HE.<sup>4-6</sup>

In the setting of our clinical practice, CTA is not currently part of the routine workup, and most ICH patients have a follow-up CT only when they develop clinical deterioration. The saying “time is brain: the outcome of stroke is generally worse the longer treatment is delayed,”<sup>7</sup> has been and continues to be a fundamental precept in ischemic stroke care. We agree that time is a key factor that relates to poor outcome in ICH patients, which means that early identification of patients at high risk for HE by initial non-contrast CT (NCCT) is important for anti-HE management.

Several NCCT markers of HE have been reported, such as irregular shape, heterogeneous density, intra-hematoma hypodensities, and hematoma sedimentation levels; however, the optimal predictor of HE on NCCT is still being debated.<sup>8-12</sup> In 2017, Shimoda et al reported the presence of a satellite sign, which they defined as a small hematoma completely separate from the main hematoma on at least one slice, on the initial NCCT that they found to be associated with a significantly worse functional outcome in ICH patients.<sup>13</sup> Later, Yu et al, using the ABC/2 method to estimate hematoma volume, suggested the satellite sign an independent predictor of HE. Although spot sign from CTA has higher predictive accuracy, the satellite sign is still an acceptable predictor of HE when CTA is unavailable.<sup>14</sup>

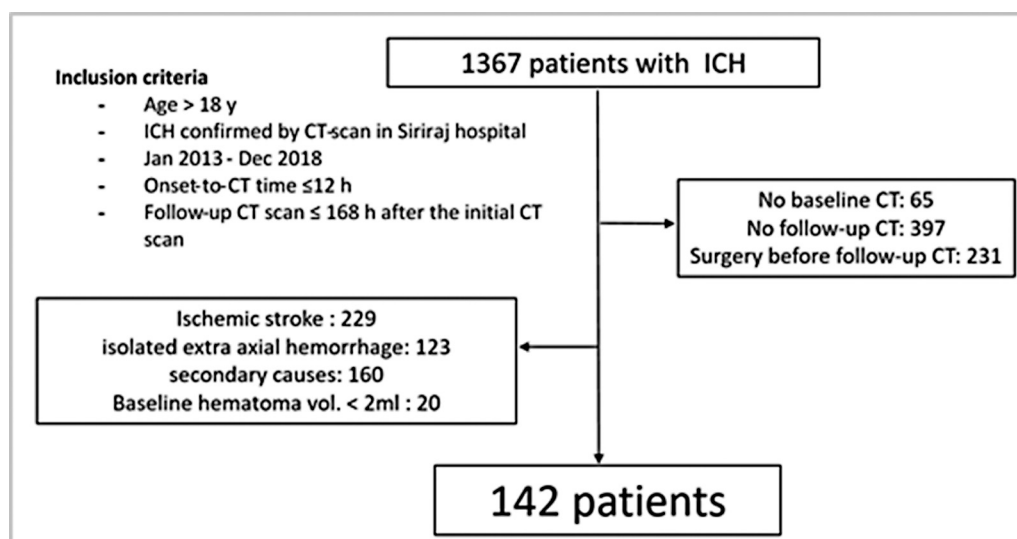
At our center, most spontaneous ICH patients receiving conservative treatment will have a follow-up CT if they demonstrate clinical deterioration or at least within 7 days. No previous study has investigated the efficacy of satellite sign for predicting HE in our population. Moreover, we postulated that using CT image analysis software to measure hematoma volume would yield more precise data and decrease inter-reader variability. Accordingly, the aim of this study was to investigate the potential of satellite sign for prediction of HE in spontaneous ICH patients who had follow-up NCCT within 7 days after the initial CT scan by using CT image analysis software to determine hematoma volume.

## Materials and Methods

### Patients

We retrospectively reviewed cases recorded in the ICH database at our hospital during January 2013 to December 2018. Cases were eligible for inclusion if they met the following criteria: (1) age of 18 years or older, (2) spontaneous ICH confirmed by CT scan, (3) onset-to-CT time 12 hours or lesser, and (4) follow-up CT scan was conducted within 168 hours or 7 days after the initial CT scan. The exclusion criteria were: (1) secondary ICH, such as hemorrhagic transformation from a cerebral infarct, cerebrovascular anomalies, tumor, or trauma; (2) unavailable baseline CT or follow-up CT; and/or (3) surgical evacuation before follow-up CT scan. A flow diagram describing the patient enrollment process is shown in ►Fig. 1. The following baseline information of spontaneous ICH patients was collected: demographic variables (age and gender), medical history (hypertension, chronic kidney disease), medication (antiplatelet drug), admission Glasgow Coma Scale score, admission blood pressure (BP) levels (systolic and diastolic), and laboratory data (platelet count, prothrombin time [PT], activated partial thromboplastin time [aPTT], and creatinine).

The protocol for this study was approved by our Institutional Review Board (SIRB) (COA no. 737/2561). The requirement to



**Fig. 1** Flow diagram of the patient enrollment process.

obtain written informed consent was waived due to the retrospective nature of this study.

### CT Imaging Technique

The CT scans performed on patients included in this study were performed on a 64-slice CT scanner (GE LightSpeed VCT) (GE Discovery) or a 256-MDCT (GE Revolution CT) (all GE Healthcare, Chicago, Illinois, United States). The CT imaging parameters were as follows: 120 kVp; 200 to 490 mA; section thickness, 1.25 mm; pitch, 1:1.

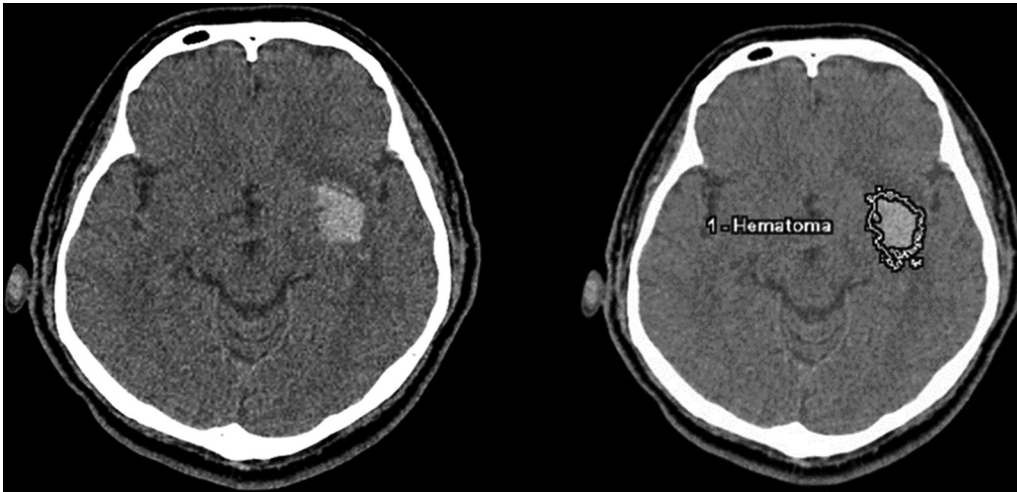
### Image Interpretation

ICH was diagnosed using axial 1.25-mm thick section images obtained from brain CT, with CT density profiles within the range established for hemorrhage based on Hounsfield units (HUs). The location of ICH was classified into the following four areas: lobar (cortex and subcortical white matter), deep (basal ganglia, thalamus, internal capsule, and deep periventricular white matter), brain stem, and cerebellum. When hemorrhage volume was large and had spread to more than

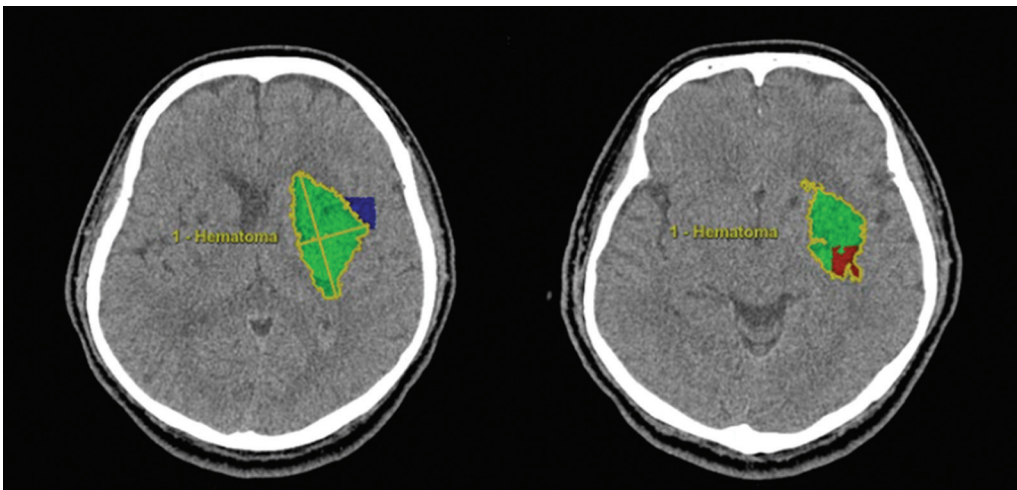
two areas, the location of ICH was defined on the basis of the area of the main hemorrhage. The onset-to-CT time and the duration from the initial CT to the follow-up CT were also recorded.

### Measurement of the Main Hemorrhage Size

Hematoma volumes on CT scans were measured by Stroke VCAR (Volume Computer-Assisted Reading) software (GE Healthcare). Stroke VCAR is a CT image analysis software package that is designed to evaluate NCCT images. Hematoma segmentation is semiautomated and is triggered by a user click. The exam is loaded and the region-of-interest (ROI) of the suspected hematoma is selected. The software then performs an automated segmentation of the ROI if the volumetric parameter falls within the hematoma HU range (→ Fig. 2). The software also provides the user with a tool called Smart Mesh to edit the hematoma segmentation results (→ Fig. 3). In cases where that hemorrhagic lesion cannot be detected automatically by the software, ROIs can be manually drawn by tracing the perimeters of the



**Fig. 2** Automated segmentation of the region of interest (ROI) based on the hematoma Hounsfield unit (HU) range.



**Fig. 3** Smart Mesh to edit the hematoma segmentation results. *Blue highlight* indicates the volume to be added to the segmented object. *Red highlight* indicates the volume to be removed.

hematoma on each slice throughout the hemorrhagic lesion. The ROIs in every slice are then summed after adjusting for slice thickness to determine the hematoma volume. Accuracy for intracerebral hematoma is 85%, with an average variation of 15% underestimation (Stroke VCAR User Guide Direction 5486219-1EN, Revision 3). Intraventricular hemorrhage (IVH), subarachnoid hemorrhage, and satellite hemorrhage, when present, were not included in the size measurement.

The minimum slice thickness and volume values supported by the hematoma segmentation are as shown in **Table 1**.

Due to the minimum support size of the software, patients with hematoma volume less than 2 mL (on initial CT) were excluded from this study.

### Hematoma Expansion

HE was defined by two methods. HE was first inspected and measured by a radiologist on the axial plane (expansion vs. non-expansion). HE was then evaluated using image analysis software to obtain the quantitative results (mL and percentage change). The association between satellite sign and each 1% increase in hematoma volume was calculated. Substantial HE (SHE), defined as absolute growth greater than 12.5 mL or relative growth greater than 33% in hematoma size, was also used to evaluate potential association with satellite sign.<sup>15</sup>

### Definition of Satellite Sign

Hemorrhages were classified into two types according to the presence or absence of a satellite sign around the main hemorrhage (**Fig. 4**). From a previous study, the criteria for satellite sign on NCCT were: (1) presence of a small

hematoma completely separate from main hematoma on at least one slice, (2) the largest transverse diameter of the small hematoma less than 10 mm, and (3) the minimal distance from the small hematoma to the main hematoma from 1 to 20 mm.<sup>1</sup> When satellite sign was questionable on axial images, coronal and sagittal reformatted images were also evaluated to obtain a more precise result. To check the accuracy of the determination of a satellite sign, two radiologist observers (D.S. and W.P.) independently evaluated each case. Any disagreement between the two reviewers was resolved by consensus.

### Statistical Analysis

Baseline characteristics were compared between patients with and without HE. Normally distributed continuous data are presented as mean and standard deviation and were compared using *t*-test. Nonnormally distributed data are presented as median and interquartile range (IQR) and were compared using Mann–Whitney *U* test. Categorical values were compared using chi-square analysis and are shown at number and proportion. Multivariable logistic regression was performed to identify factors independently associated with HE. The results of that analysis are shown as adjusted odds ratio and 95% confidence interval. Inter-reader reliability for the identification of satellite sign was analyzed using  $\kappa$  values. A *p*-value of less than 0.05 indicates statistical significance. All statistical analyses were performed using SPSS 22.0 and Excel 2013.

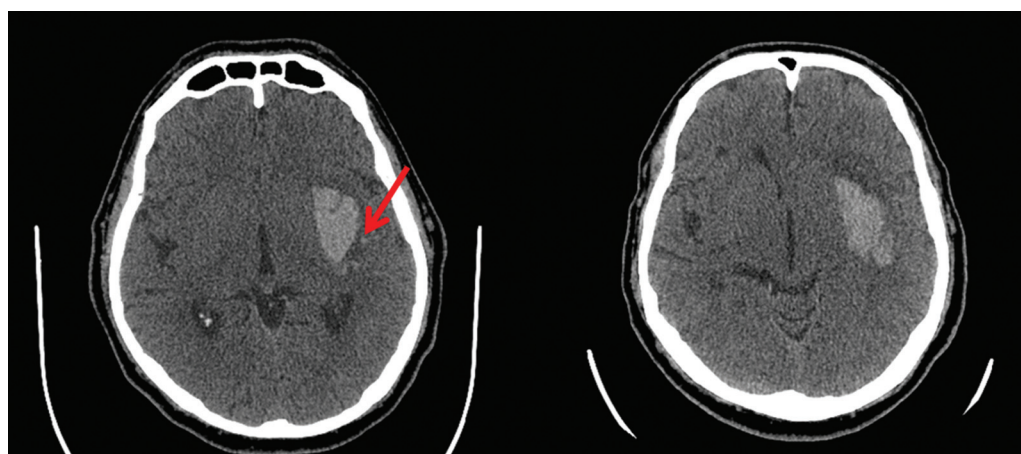
## Results

### Patient Characteristics

There were 1,367 patients that were diagnosed with ICH during the study period. Of those, 229 patients had ischemic stroke with hemorrhagic transformation, 123 patients had isolated extra-axial hemorrhage, and 160 patients had secondary causes. The remaining 855 patients with a diagnosis of primary ICH were screened for inclusion eligibility. Of those, 713 patients were excluded for the following reasons: no baseline cranial CT within 12 hours of symptom onset ( $n = 65$ ), no follow-up CT

**Table 1** Minimum slice thickness and volume values supported by the hematoma segmentation

Slice Thickness (St) Range (in mm)	Minimum Supported Size (Volume in cm <sup>3</sup> )
$St < 2.5$	2
$2.5 \leq St \leq 5$	5



**Fig. 4** Example of positive satellite sign on non-contrast computed tomography (NCCT) in patient with intracerebral hemorrhage that had hematoma expansion on the follow-up NCCT on day 5.

**Table 2** Characteristics of the entire study cohort, and compared between patients without and with hematoma expansion (HE)

Characteristics	Total (n = 142)		Without HE (n = 97)		With HE (n = 45)		p-Value
Age (y), mean (SD)	62.1	(13.7)	62.9	(12.6)	60.40	(15.8)	0.315
Male gender, n (%)	90	(63.4)	63	(64.9)	27	(60.0)	0.569
Hypertension, n (%)	114	(80.3)	79	(81.4)	35	(77.8)	0.609
Chronic kidney disease, <sup>a</sup> n (%)	8	(5.6)	4	(4.1)	4	(8.9)	0.252
Antiplatelet use, n (%)	27	(19.0)	17	(17.5)	10	(22.2)	0.507
SBP (mm Hg), mean (SD)	170.9	(35.5)	173.3	(33.7)	165.9	(38.9)	0.253
DBP (mm Hg), mean (SD)	96.4	(20.1)	97.9	(19.0)	93.1	(22.1)	0.186
GCS score, mean (SD)	13.0	(3.0)	13.0	(3.0)	13.0	(3.0)	0.947
Platelet count ( $\times 10^9/L$ ), mean (SD)	234.2	(87.7)	241.3	(82.3)	218.7	(97.7)	0.154
PT (s), median (IQR)	11.9	(9.9–76.7)	11.9	(9.9–59.0)	12.0	(10.3–76.7)	0.440
aPTT (s), mean (SD)	26.0	(7.8)	24.6	(4.9)	29.2	(11.3)	<b>0.001</b>
Creatinine (mg/dL), median (IQR)	0.9	(0.4–12.1)	0.8	(0.4–8.6)	0.9	(0.4–12.1)	0.202
Onset time <sup>b</sup> (h), median (IQR)	3.0	(1–12)	3.0	(1–12)	2.5	(1–11)	0.343
Follow-up time <sup>c</sup> (h), median (IQR)	44.5	(3–168)	60.0	(4–168)	22.0	(3–168)	<b>0.001</b>
Baseline hematoma volume (mL), median (IQR)	16.7	(2.1–79.5)	11.7	(2.1–79.5)	27.4	(2.9–59.3)	<b>0.001</b>
Hematoma location, n (%)							<b>0.019</b>
Lobar	36	(25.4)	19	(19.6)	17	(37.8)	
Deep	94	(66.2)	68	(70.1)	26	(57.8)	
Brainstem	2	(1.4)	1	(1.0)	1	(2.2)	
Cerebellum	10	(7.0)	9	(9.3)	1	(2.2)	
Lobar (vs. non-lobar)	36	(25.4)	19	(19.6)	17	(37.8)	<b>0.020</b>
Satellite sign, n (%)	62	(43.7)	36	(37.1)	26	(57.8)	<b>0.021</b>
Intraventricular hemorrhage, n (%)	65	(45.8)	50	(51.5)	15	(33.3)	<b>0.043</b>

Abbreviations: aPTT, activated partial thromboplastin time; CT, computed tomography; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; IQR, interquartile range; SBP, systolic blood pressure; SD, standard deviation; PT, prothrombin time.

Note: A *p*-value of < 0.05 indicates statistical significance, as highlighted in bold values.

<sup>a</sup>Chronic kidney disease was defined as estimated glomerular filtration rate < 60 mL/min.

<sup>b</sup>Time from onset to baseline CT.

<sup>c</sup>Time from baseline CT to follow-up CT.

within 168 hours after the baseline CT (*n* = 397), hematoma evacuation before the follow-up CT (*n* = 231), and initial hematoma volume less than 2 mL, which is the minimum volume that can be measured by the image analysis software (*n* = 20). The remaining 142 patients were included in this study.

The characteristics of the study cohort are shown in **Table 2**. The mean age of the patients was  $62.1 \pm 13.7$  years, and 63.4% were men. The median time from onset to baseline CT was 3 hours (range: 0–12). The median time from follow-up to baseline CT was 44.5 hours (range: 3–168). The median baseline hematoma volume was 16.7 mL (range: 2.1–79.5).

### Hematoma Expansion

**Table 2** lists the results of univariate comparisons between patients with and without HE. Patients with HE had significantly higher mean aPTT ( $29.2 \pm 11.3$  vs.  $24.6 \pm 4.9$ , respectively; *p* = 0.001) and median baseline hematoma volume (27.4 [IQR: 2.9–59.3] vs. 11.7 mL [IQR: 2.1–79.5]; *p* = 0.001). Lobar location was significantly more common in patients

with HE (37.8 vs. 19.6%; *p* = 0.02). Time from baseline CT to follow-up CT was significantly shorter in patients with HE (22 vs. 60 hours; *p* = 0.001). ICH patients with IVH had significantly less HE than patients without IVH (*p* = 0.043).

### Satellite Sign

The prevalence of satellite sign in this study was 43.7%. The prevalence of satellite sign was significantly higher in patients with HE than in those without HE (57.8%, *p* = 0.021). Overall agreement for identifying a satellite sign between the two readers in this study was very good (Cohen's kappa: 0.81). The results of analysis for association between satellite sign and other factors are shown in **Table 3**. Patients with satellite sign had significantly higher aPTT (*p* = 0.001) and baseline volume (31.3 mL, *p* = 0.001). Time from baseline CT to follow-up CT was significantly shorter in patients with satellite sign (*p* = 0.001). Patients with IVH had a significantly lower prevalence of satellite sign than patients without IVH (*p* = 0.001). Lobar location was significantly more common in patients with

**Table 3** Characteristics of the entire study cohort, and compared between patients without and with satellite sign

Characteristics	Total (n = 142)		Without satellite sign (n = 80)		With satellite sign (n = 62)		p-Value
Age (y), mean (SD)	62.1	(13.7)	60.6	(13.0–58.0)	64.0	(14.5)	0.315
Male gender, n (%)	90	(63.4)	56	(70.0)	34	(54.8)	0.063
Hypertension, n (%)	114	(80.3)	67	(83.8)	47	(25.8)	0.238
Chronic kidney disease, <sup>a</sup> n (%)	8	(5.6)	3	(3.8)	5	(8.1)	0.269
Antiplatelet use, n (%)	27	(19.0)	13	(16.3)	14	(22.6)	0.340
SBP (mm Hg), mean (SD)	170.9	(35.5)	171.9	(33.7)	169.9	(37.9)	0.253
DBP (mm Hg), mean (SD)	96.4	(20.1)	98.9	(19.1)	93.2	(21.0)	0.186
GCS score, mean (SD)	13.0	(3.0)	13.0	(3.0)	13.0	(3.0)	0.947
Platelet count ( $\times 10^9/L$ ), mean (SD)	234.1	(87.7)	237.0	(82.5)	230.2	(94.6)	0.154
PT (s), median (IQR)	11.9	(9.9–76.7)	11.8	(10.3–76.7)	12.1	(9.9–66.5)	0.440
aPTT (s), mean (SD)	26.0	(7.8)	25.1	(5.8)	27.2	(9.8)	<b>0.001</b>
Creatinine (mg/dL), median (IQR)	0.9	(0.4–12.1)	0.9	(0.4–8.6)	0.9	(0.4–12.1)	0.202
Onset time <sup>b</sup> (h), median (IQR)	3.0	(1–12)	3.0	(1–12)	3.0	(1–12)	0.343
Follow-up time <sup>c</sup> (h), median (IQR)	44.5	(3–168)	51.5	(3–168)	39.0	(4–168)	<b>0.001</b>
Baseline hematoma volume (mL), median (IQR)	16.7	(2.1–79.5)	9.9	(2.1–57.4)	31.3	(3.4–79.5)	<b>0.001</b>
Hematoma location, n (%)							<b>0.001</b>
Lobar	36	(25.4)	12	(15.0)	24	(38.7)	
Deep	94	(66.2)	58	(72.5)	36	(58.1)	
Brainstem	2	(1.4)	2	(2.5)	0	(0.0)	
Cerebellum	10	(7.0)	8	(10.0)	2	(3.2)	
Lobar (vs. non-lobar)	36	(25.4)	12	(15.0)	24	(38.7)	<b>0.001</b>
Intraventricular hemorrhage, n (%)	65	(45.8)	46	(57.5)	19	(30.6)	<b>0.001</b>

Abbreviations: aPTT, activated partial thromboplastin time; CT, computed tomography; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; IQR, interquartile range; PT, prothrombin time; SBP, systolic blood pressure; SD, standard deviation.

Note: A *p*-value of < 0.05 indicates statistical significance, as highlighted in bold values.

<sup>a</sup>Chronic kidney disease was defined as estimated glomerular filtration rate < 60 mL/min.

<sup>b</sup>Time from onset to baseline CT.

<sup>c</sup>Time from baseline CT to follow-up CT.

**Table 4** Multivariate logistic regression model for factors that predict hematoma expansion

Factors	OR	95% CI		p-Value
		Lower	Upper	
Activated partial thromboplastin time (aPTT)	1.078	1.000	1.163	0.050
Lobar hematoma location	1.525	0.600	3.876	0.375
Follow-up time <sup>a</sup> for every 1-h increase	0.991	0.982	0.999	<b>0.032</b>
Baseline hematoma volume for every 1-mL increase	1.013	0.986	1.040	0.349
Satellite sign	2.495	1.162	5.354	<b>0.019</b>
Intraventricular hemorrhage	0.785	0.338	1.822	0.573

Abbreviations: CI, confidence interval; CT, computed tomography; OR, odds ratio.

Note: A *p*-value of < 0.05 indicates statistical significance, as highlighted in bold values.

<sup>a</sup>Time from baseline CT to follow-up CT.

satellite sign (*p* = 0.001). Multivariate analysis revealed satellite sign to be independently associated with HE (**Table 4**).

The sensitivity, specificity, and accuracy of satellite sign for predicting HE was 57.8, 62.9, and 61.3%, respectively. From

image analysis software, the cutoff of more than 9% relative growth in hematoma volume on follow-up NCCT showed the strongest association with satellite sign (*p* = 0.024), with a sensitivity of 55%, specificity of 64.6%, and accuracy of 60.5%.

However, satellite sign was not statistically significant associated with SHE ( $p = 0.941$ ).

## Discussion

HE is the most important modifiable predictor that can change the outcome of ICH.<sup>3</sup> Our population had a mean age of 62.1 years, and 63.4% were men. Univariate analysis revealed high aPTT, short follow-up time, large initial hematoma volume, and absence of IVH to be significantly associated with HE. However, multivariate analysis showed only follow-up time and satellite sign to be independent predictors of HE (this will be discussed in more detail below). Other factors, such as time from onset to baseline CT, hypertension, chronic kidney disease, antiplatelet use, BP on admission, platelet count, PT, and creatinine, were not found to be significantly associated with HE in this study. These results are similar to many previous ICH studies.<sup>16–19</sup>

No generally accepted cutoff for change in hematoma volume has yet been established for HE. In 1997, Brott et al studied 142 ICH patients who underwent a baseline CT within 3 hours after clinical onset, and that had follow-up CTs at 1 and 20 hours after baseline CT. They prospectively selected 33% change in hematoma volume as measured by image analysis to be the cutoff for HE, and they found it to be significantly associated with early neurological deterioration. Subsequent studies have used this cutoff to define SHE. Furthermore, they found that most ongoing bleeding occurred within 3 to 4 hours after hemorrhage onset, and they found this to also be significantly associated with early neurological deterioration.<sup>20</sup> Thus, early identification of patients at risk for HE is crucial. Many NCCT predictors have been proposed, but they are still controversial, and they have overlapping definitions.<sup>8–12</sup>

In 2017, Shimoda et al coined the term “satellite sign” to describe a new NCCT marker, which was defined as a small hematoma completely separate from the main hematoma on at least one slice. They retrospectively reviewed 241 ICH patients who underwent NCCT within 12 hours after clinical onset, and they found the satellite sign to be associated with a significantly worse functional outcome in ICH patients.<sup>13</sup>

Later, Yu et al studied 153 ICH patients who underwent a baseline CT within 6 hours after clinical onset and a follow-up CT within 24 hours after baseline CT. They used the ABC/2 method to calculate the hematoma volume, and they defined absolute growth greater than 12.5 ml or relative growth greater than 33% in hematoma size on follow-up CT as HE, which occurred in 37 patients or 24% of all study patients. The sensitivity, specificity, positive predictive value, and negative predictive value of satellite sign for HE prediction in their study was 59.46, 68.97, 37.93, and 84.21%, respectively. They reported the satellite sign to be an independent predictor of spontaneous ICH, and they suggested satellite sign as being an acceptable predictor of HE when CTA is unavailable.<sup>14</sup>

The clear definition, the ease of use, and the potential for predicting HE reported in the previous study of satellite sign compelled us to investigate this NCCT sign among our ICH

population. None has been done before. The very good agreement for determining a satellite sign between the two readers in our study (Cohen's kappa: 0.81) confirmed that satellite sign has clear definition and is practical for use in routine clinical practice. In 142 patients, we found satellite sign to be significantly associated with HE, but not significantly associated with SHE (defined as absolute growth > 12.5 ml or relative growth > 33% in hematoma size). So, the cutoff of HE is the key factor that influences differences in results among studies. Our patients had NCCT within 12 hours from onset, which is the same timing that was used in the Shimoda et al study. However, in our country, there is no definite guideline for optimal timing of follow-up CT. Most ICH patients with conservative treatment will undergo follow-up CT when they develop clinical deterioration or at least within 7 days after the initial CT. Accordingly, we included patients with follow-up CT within 7 days in our study since it reflects real-life clinical practice in the study. This timing was markedly different from many previous ICH studies, especially from a study by Brott et al that first defined SHE in ICH patients having 1- and 20-hour follow-up CTs.

In our study, the median time from baseline CT to follow-up CT was 46 hours (range 3–168 hours). Fifty-three patients (37%) had follow-up CT within 24 hours, and 43.3% of those patients had HE. The other 89 patients (63% of all patients) had a 22.6% prevalence of HE. These data confirm the finding of several previous studies in ICH that ongoing bleed occurred during the first several hours.<sup>16–19</sup> However, there were 20 patients (44.4% of patients with HE) who had HE after 24 hours, and 10 of those (22.2% of patients with HE) had percentage expansion less than 33%. In addition, our study cohort had less baseline hematoma volume than the cohort of Yu et al (16.7 vs. 24.7 mL, respectively), and lower baseline hematoma volume normally expands less and less often than higher baseline hematoma volume. As such, the cutoff of more than 33% hematoma growth was not the optimal cutoff value in our study.

Qualitative measurement to determine expansion versus non-expansion was initially and independently performed by two radiologists, after which image analysis software was used to obtain quantitative results, which is the same quantitative method used by Brott et al. We decided to use image analysis software because we felt that it would deliver more precise data and decrease inter-reader variability.

The association between satellite sign and each 1% increase in hematoma volume was calculated, and we found the cutoff of greater than 9% relative growth in hematoma volume on follow-up NCCT have the strongest association with satellite sign ( $p = 0.024$ ). The sensitivity, specificity, and accuracy were 55.0, 64.6, and 60.5%. The 9% cutoff found in this study is lower than the previously reported cutoff of 33%.

## Limitations

This study has some limitations. First, our study's retrospective design made it susceptible to incomplete or missing data. Second, the fact that our data came from a single center that

is also a national tertiary referral center suggests that our findings may not be immediately generalizable to all other care settings. Third, we did not investigate the accuracy of Stroke VCAR in this study. Fourth, our small sample size may have limited our study's ability to identify all significant differences and correlations. Fifth, other factors during hospitalization, such as BP control and antithrombotic drug use, were not included in our analysis. Sixth and last, an insufficient amount of data prevented us from investigating association between the new HE cutoff value and clinical outcomes.

## Conclusion

Satellite sign, a new NCCT predictor, was found to be significantly associated with HE. With different context of Thai population, HE was found in smaller baseline hematoma volume. Satellite sign was found more common in lobar hematoma ( $p=0.001$ ) and less common in patients with IVH ( $p=0.001$ ). Quantitative measurement by image analysis software revealed HE greater than 9%, different from standard greater than 33%, to have the strongest association with satellite sign. Using software analysis might better help detection HE. Further studies to validate satellite sign for predicting HE and to identify an optimal cutoff in our population that is correlated with clinical outcomes are warranted.

### Ethics Approval

The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB) (COA no. 737/2561) of Mahidol University that was certified and is in full compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines, and the international Conference on Harmonization in Good Clinical Practice (ICH-GCP). The requirement to obtain written informed consent was waived due to the retrospective nature of this study.

### Conflict of Interest

None declared.

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