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FULL RESEARCH ARTICLE

Hounsfield units on noncontrast computed tomography predict hematoma expansion in patients with intracerebral hemorrhage

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ABSTRACT

Introduction: *Hounsfield units (HU) have been proposed as a prognostic marker of hematoma expansion in patients with intracerebral hemorrhage (ICH). The aim of this study was to determine the optimal HU value for predicting hematoma expansion on noncontrast computed tomography (NCCT) in patients diagnosed with ICH.* **Material and Methods:** *Prospective cohort study of patients with ICH. Baseline cranial NCCT was performed within 8 hours of symptom onset and an NCCT follow-up within 72 hours of the baseline examination. HU and the shape and density of the hematoma were assessed at baseline NCCT. The optimal HU cut-off value for predicting hematoma expansion was determined by ROC analysis.* **Results:** *Fifty patients diagnosed with ICH were included. There were 28 (56.0%) men and 22 (44.0%) women. Their mean age was 57.8 ± 16.97 years. Hematoma expansion was present in 14 (28.0%) cases. At baseline NCCT, the mean HU was significantly lower in patients with expansion (61.1 ± 2.8) than in patients without hematoma expansion (69.2 ± 5.5) ($p < 0.001$). A value equal to or less than 64.2 HU on baseline NCCT was defined as the optimal cut-off point for predicting hematoma expansion. Sensitivity was 78.6%, specificity 86.1%, and the AUC was 0.914 (95% CI, 0.834-0.993) ($p < 0.001$).* **Conclusion:** *In this study, for the first time, a value equal to or less than 64.2 HU by ROC analysis on baseline NCCT was defined as the optimal cut-off point for predicting hematoma expansion in patients with ICH.*

Keywords: *Cerebral hemorrhage. Hounsfield units. Hematoma expansion. Computed tomography.*

INTRODUCTION

Intracerebral hemorrhage (ICH) is a severe stroke with high mortality of up to 40% at 30 days, and only one in five survivors is independent at 6 months[1,2]. One of the main factors associated with high mortality is hematoma expansion, which can occur in the first 24 hours after the onset of ICH[3-6]. Factors associated with hematoma expansion are related to the patient (low hemoglobin, hematocrit, and platelet count or anticoagulant therapy)[3,5,7-9] and hematoma characteristics on NCCT at baseline (initial volume, shape, and density of the hematoma)[1,3,5,10,11].

In patients without hematoma expansion, clot contraction occurs due to the contractile force generated by the interaction of fibrin and platelets, which causes the packing of red blood cells in the hematoma. Clot contraction results in an increased hematocrit with higher HU[5,7]. In contrast, a relationship between a lower HU value and hematoma expansion on baseline NCCT in the first 6 to 8 hours after the onset of ICH has been

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reported[5,7]. However, this fact has not been sufficiently studied. In addition, the HU value for predicting hematoma expansion in patients with ICH has not been defined. Thus, this study determined by ROC analysis the optimal HU value for predicting hematoma expansion on baseline NCCT in patients with ICH.

MATERIAL AND METHODS

This prospective cohort study was conducted from August 2020 to August 2022 in the Department of Radiology and Imaging and the Department of Neurosurgery of the Specialties Hospital, West National Medical Center of the Mexican Institute of Social Security in Guadalajara, Jalisco, Mexico. Patients with a diagnosis of ICH, a baseline cranial NCCT within the first 8 hours of symptom onset, and a follow-up NCCT within 72 hours of the first imaging examination were included. Patients who underwent hematoma evacuation before the follow-up NCCT, patients without a follow-up NCCT or with an MRI at follow-up, or with isolated intraventricular hemorrhage were excluded. Informed consent was not required for data obtained during routine medical care. The protocol was approved by institutional research ethics and research committees.

Study variables

Data regarding sex, age, comorbidities (systemic hypertension, diabetes mellitus, chronic kidney disease, dyslipidemia, and eclampsia), anticoagulant therapy, hemoglobin (g/dL), platelet count (10^9/L), 30-day mortality, time (hours) from the onset of symptoms to NCCT at baseline, and time between baseline and follow-up NCCT, location of hematoma, initial hematoma volume (mL), change in initial volume at follow-up NCCT (mL), percent change in volume between baseline and follow-up NCCT, HU of hematoma at baseline NCCT, and the presence of intraventricular hemorrhage were collected.

The shape (irregular, island sign, satellite sign) and density characteristics (fluid level, blend sign, black hole sign, hypodensity, swirl sign, heterogeneous density) of the hematoma on the baseline NCCT were recorded.

Definitions

Hematoma expansion: relative hematoma growth > 33% or absolute growth > 6 ml[3,7].

Irregular shape: ≥ 2 margin irregularities, connected or without hematoma borders, and rated on the axial NCCT slice with the largest hemorrhage surface[3].

Island sign: ≥ 3 scattered small bleedings, all separate from the hemorrhage, or ≥ 4 small hematomas that may be connected with the main hemorrhage[3].

Satellite sign: small hemorrhage (maximum diameter < 10 mm) that is not connected to the main hematoma, with a clear separation (1-20 mm distance)[3].

Subarachnoid hemorrhage: extension of parenchymal hemorrhage into the subarachnoid space; associated with hematoma expansion only in lobar hemorrhages[3].

Fluid level: a hypoattenuating area above and a hyperattenuating area below a straight line of separation[3].

Blend sign: hypoattenuating area adjacent to a hyperattenuating area, a clear margin between the two regions, and a density difference greater than 18 HU[3].

Black hole sign: hypoattenuating region encapsulated in the hemorrhage with a density difference > 28 HU (compared to the surrounding hemorrhage)[3].

Hypodensity: any hypodense region within the hemorrhage without a connection to surrounding structures; does not require density measurement and can be detected by visual inspection[3].

Swirl sign: any region of hypoattenuation or isoattenuation compared to the brain parenchyma, encapsulated or not in the hematoma, with any morphology[3].

Heterogeneous density: ≥ 3 regions of low attenuation compared with hemorrhage, assessed at the axial slice with the largest hematoma area[3].

ICH score: defined based on Hemphill et al.[12]

Image acquisition and analysis protocol

A Brilliance™ 64-detector tomograph (Phillips Medical Systems, Amsterdam, The Netherlands) or a Lightspeed VCT™ 32-detector tomograph (General Electric, Boston, MA, USA) was used with the following parameters: 120 kVp, 190-250 mA, with 5-mm slice thickness reconstruction. Data were analyzed using the PACS Digital Archiving System with Agfa HealthCare software™ (Agfa-Gevaert Group, Mortsel, Belgium). HU were determined in the axial plane, covering the largest area in the region of interest of the hematoma, and its volume was calculated by manual volumetry using the abc/2 equation[6]. Images were evaluated by a radiologist (DBM) with 10 years of experience.

Statistical analysis

The mean, standard deviation, minimum, maximum, and median were calculated for quantitative variables. The chi-square test or Fisher's exact test was used for categorical variables. The groups in each category were

Table 1. Characteristics of patients with diagnosis of ICH with and without hematoma expansion

Parameters	Hematoma expansion			p value
	Total (n = 50)	No (n = 36)	Yes (n = 14)	
Men, n (%)	28	22 (61.1)	6 (42.8)	0.252
Women, n (%)	22	14 (38.9)	8 (57.2)	0.355
Age, years	57.8 ± 16.97 (22, 58, 89)	58.2 ± 16.07 (24, 58, 89)	56.7 ± 19.70 (22, 58.5, 87)	0.885
Comorbidities				
HTA, n (%)	43 (86.0)	33 (91.7)	10 (71.4)	0.085
Diabetes mellitus, n (%)	18 (36.0)	15 (41.7)	3 (21.4)	0.181
Chronic kidney disease, n (%)	5 (10.0)	4 (11.1)	1 (7.1)	0.675
Dyslipidemia, n (%)	1 (2.0)	0	1 (7.1)	0.280
Eclampsia, n (%)	3 (6.0)	2 (5.6)	1 (7.1)	1.000
Anticoagulant treatment, n (%)	3 (6.0)	1 (2.8)	2 (14.3)	0.186
Laboratory tests				
Hemoglobin g/dL	12.95 ± 2.78 (6, 13.5, 17.6)	12.97 ± 2.87 (6, 13.35, 17.6)	12.90 ± 2.65 (7.2, 13.55, 16.5)	0.953
Platelet count, 10^9/L	239.46 ± 86.49 (30, 244.5, 446)	260.47 ± 72.79 (118, 254.5, 446)	185.43 ± 97.82 (30, 189.5, 314)	0.016
Mortality after 30 days				
No, n (%)	33 (66.0)	24 (66.7)	9 (64.3)	1.000
Yes, n (%)	17 (34.0)	12 (33.3)	5 (35.7)	

ICH: intracerebral hemorrhage; NCCT: noncontrast computed tomography; HTA: hypertension arterial. Values are given as mean, standard deviation, minimum, median and maximum, unless otherwise indicated.

compared using the z-test for proportions, correcting the p-value with the Bonferroni method. Student's t-test and the Mann-Whitney U test were used to evaluate the statistical significance of quantitative variables between patients with and without hematoma expansion. Multivariate logistic regression of significant variables was performed to predict hematoma expansion. The optimal cut-off point for HU to predict hematoma expansion was defined by ROC analysis. A p-value < 0.05 was considered significant. IBM-SPSS version 25 (IBM Corp., Armonk, NY, USA) was used for data analysis.

RESULTS

Fifty patients diagnosed with ICH were included. There were 28 (56.0%) men and 22 (44.0%) women with a mean age of 57.8 ± 16.97 years (range, 22 to 89). The characteristics of patients with and without hematoma expansion are shown in Table 1. Hematoma expansion was present in 14 (28.0%) of the 50 patients, 8 women and 6 men. The most common comorbidities were systemic arterial hypertension (n = 43, 86.0%) and diabetes mellitus (n = 18, 36.0%), and there were no significant differences in age, sex, and comorbidities in patients with and without hematoma expansion. The platelet count was significantly lower in patients with hematoma expansion (mean 185.43 ± 97.82 × 10^9/L) compared to patients without hematoma expansion (mean 260.47 ± 72.79 × 10^9/L) (p = 0.016). Mortality at 30 days after ICH was comparable between patients with and without hematoma expansion. The ICH score showed no significant difference between both groups (Table 2).

Baseline NCCT was performed with a mean of 6.4 ± 1.26 hours after the onset of ICH symptoms, whereas the time between baseline NCCT and follow-up NCCT was 30.0 ± 16.33 hours (Table 3). The most common locations of hematomas were lobar (n = 19, 38.0%) and thalamic (n = 19, 38.0%). The mean baseline NCCT HU value was significantly lower in patients with expansion (61.1 ± 2.8) than in cases without expansion (69.2 ± 5.5) (p < 0.001). The ROC analysis defined a value equal to or less than 64.2 HU as the optimal cut-off point for predicting hematoma expansion on baseline NCCT in patients with ICH (Figure 1A). Sensitivity was

Table 2. ICH score[a] in patients with diagnosis of ICH with and without hematoma expansion

ICH score	Total (n = 50) n (%)	Hematoma expansion		p value
		No (n = 36) n (%)	Yes (n = 14) n (%)	
0	1 (2.0)	1 (2.8)	0 (0)	1.000
1	26 (52.0)	20 (55.6)	6 (42.9)	1.000
2	7 (14.0)	4 (11.1)	3 (21.4)	0.306
3	10 (20.0)	7 (19.4)	3 (21.4)	0.668
4	5 (10.0)	3 (8.3)	2 (14.3)	0.436
5	1 (2.0)	1 (2.8)	0 (0)	1.000

[a]Hemphill et al.[12]. ICH. intracerebral hemorrhage.

Table 3. NCCT features in patients with diagnosis of ICH with and without hematoma expansion

Parameters	Total (n = 50)	Hematoma expansion		p value
		No (n = 36)	Yes (n = 14)	
Time from onset of symptoms to baseline NCCT, hours	6.4 ± 1.26 (4, 7, 8)	6.3 ± 1.22 (4, 6, 8)	6.6 ± 1.40 (4, 7, 8)	0.448
Time between first and follow-up NCCT, hours	30.0 ± 16.33 (2, 26.5, 71)	32.1 ± 16.90 (2, 27.5, 71)	24.8 ± 13.97 (7, 23.5, 55)	0.144
Location of hematoma				0.101
Lobar, n (%)	19 (38.0)	10 (27.8)	9 (64.3)	0.653
Thalamic, n (%)	19 (38.0)	16 (44.4)	3 (21.4)	0.476
Ganglios, n (%)	9 (18)	8 (22.2)	1 (7.1)	0.392
Infratentorial, n (%)	3 (6.0)	2 (5.6)	1 (7.1)	1.000
HU of the hematoma at baseline NCCT	66.9 ± 6.1 (57.7, 65.6, 82.0)	69.2 ± 5.5 (58.6, 67.8, 82.0)	61.1 ± 2.8 (57.7, 60.1, 65.8)	< 0.001
Initial hematoma volume at baseline NCCT mL	26.16 ± 17.94 (2.32, 23.02, 83.88)	25.75 ± 18.67 (2.32, 22.87, 83.88)	27.22 ± 16.54 (2.55, 26.22, 63.02)	0.487
Change in hematoma volume at follow-up NCCT, mL	1.53 ± 9.49 (–19.33, 0.0, 36.05)	–2.50 ± 5.01 (–19.33, –1.8, 5.52)	11.90 ± 10.55 (3.5, 8.3, 36.05)	< 0.001
Percent change in hematoma volume between baseline and follow-up NCCT, %	8.14 ± 39.80 (–48.3, –0.15, 159.46)	–9.78 ± 18.91 (–48.3, –8.5, 18.1)	54.2 ± 42.81 (18.5, 38.8, 159.5)	< 0.001
Intraventricular hemorrhage, n (%)	29 (58.0)	22 (61.1)	7 (50.0)	0.475

NCCT: noncontrast CT; HU: Hounsfield units, mL: milliliters. Values are given as mean, standard deviation, minimum, median and maximum, unless otherwise indicated.

78.6%, specificity 86.1%, and the area under the curve (AUC) was 0.914 (95% CI, 0.834-0.993) (p < 0.001). The maximum sensitivity/specificity point corresponds to 64.2 HU to discriminate between patients with and without hematoma expansion (Figure 1B).

The mean initial hematoma volume was 25.75 ± 18.67 mL in patients without expansion compared to 27.22 ± 16.54 mL in patients with hematoma expansion (p: ns). In contrast, the volume increase and percent change in volume in follow-up NCCT showed significant differences between patients with and without expansion (p < 0.001).

Figure 2 shows the baseline NCCT of a 37-year-old man with ICH and a lobar hematoma of 61.0 HU. The follow-up CT shows the expansion of the hematoma. In contrast, Figure 3 shows a 69-year-old woman with ICH and a lobar hematoma. Baseline NCCT showed a hematoma of 65.0 HU, and the follow-up CT showed no hematoma expansion.

Table 4 shows the hematoma shape and density characteristics at baseline NCCT. Irregular shape and hypodensity were present in all cases (n = 14, 100%) with hematoma expansion. Significant differences

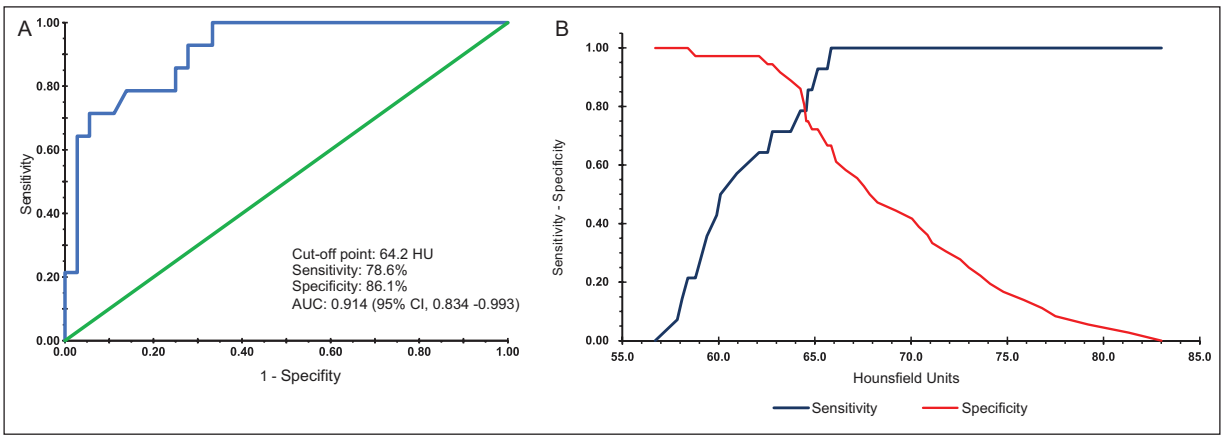


Figure 1. A: ROC analysis shows that the value equal to or less than 64.2 HU is the optimal cut-off point in the baseline NCCT for predicting hematoma expansion in patients with ICH. **B:** sensitivity/specificity analysis for HU as a marker in baseline NCCT of hematoma expansion in patients with ICH. The point of maximum sensitivity/specificity corresponds to the intersection of the two curves for distinguishing between patients with and without hematoma expansion.

NCCT: noncontrast CT; HU: Hounsfield units; ICH: intracerebral hemorrhage; ROC: receiver operating characteristic.

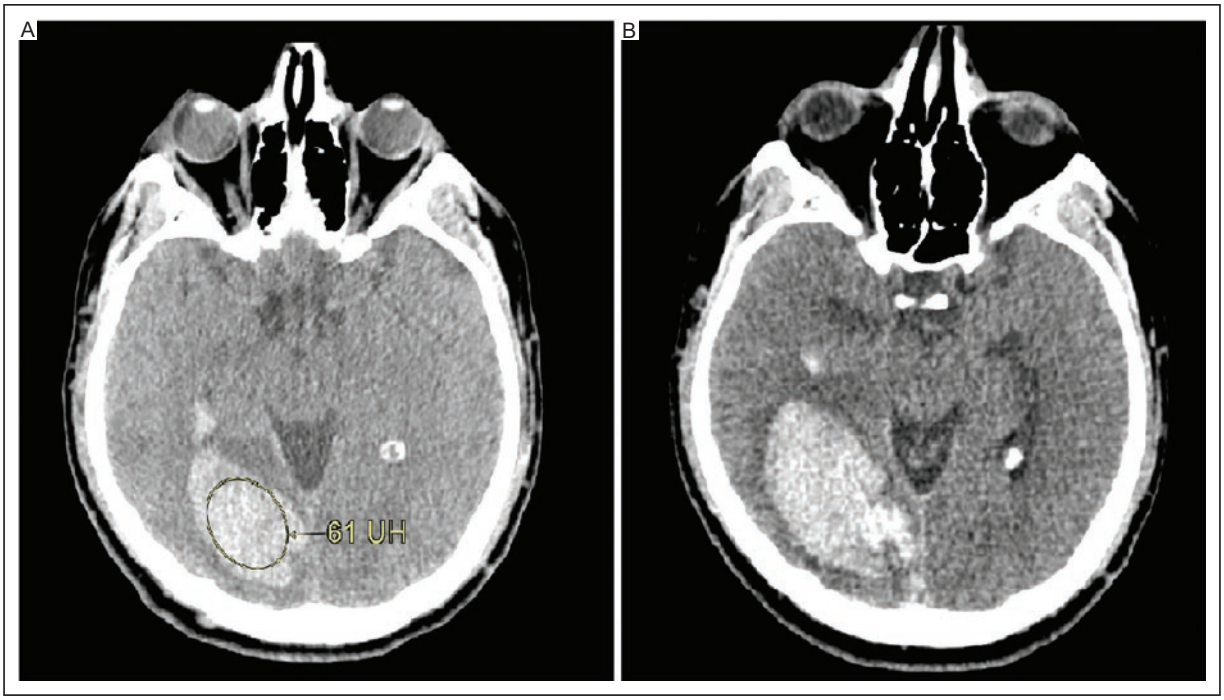


Figure 2. Axial NCCT of a 37-year-old man treated with oral anticoagulants for prosthetic heart valve: Lobar ICH, score 1. **A:** baseline NCCT, 7 hours after symptom onset, showing right occipital intraparenchymal hematoma with an initial volume of 39.5 mL and a mean attenuation coefficient of 61.0 HU. **B:** follow-up NCCT 24 hours after baseline NCCT showing hematoma expansion with a volume of 80.1 mL.

NCCT: noncontrast CT; HU: Hounsfield units; ICH: intracerebral hemorrhage; mL: milliliters.

between patients with and without hematoma expansion were observed as irregular shape, black hole, hypodensity, and swirl. Shape characteristics in baseline NCCT are shown in Figure 4, and density characteristics in Figures 5 and 6.

Only HU and a lower platelet count were significant in the multivariate binary logistic regression predicting the risk of hematoma expansion in baseline NCCT. In contrast, shape and density features lost significance in the final multivariate model.

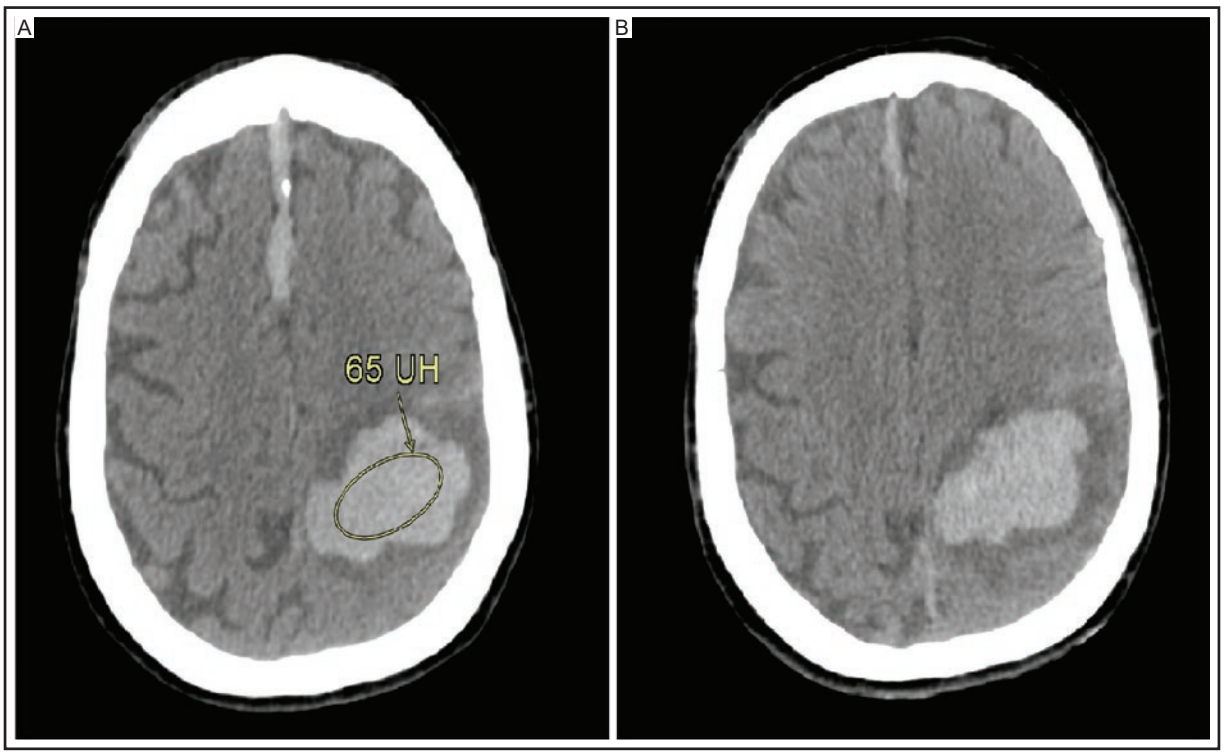


Figure 3. Axial NCCT of a 69-year-old woman with systemic arterial hypertension and T2 diabetes mellitus. Lobar ICH, score 1. **A:** baseline NCCT, 7 hours after symptom onset, showing left frontoparietal intraparenchymal hematoma with an initial volume of 41.7 mL and a mean attenuation coefficient of 65.0 HU. **B:** follow-up NCCT at 14 hours after baseline NCCT showed no expansion of the hematoma with a volume of 40.6 mL.

NCCT: noncontrast CT; HU: Hounsfield units; ICH: intracerebral hemorrhage; mL: milliliters.

Table 4. Shape and density features at baseline NCCT in patients with diagnosis of ICH with and without hematoma expansion

Parameters	Total (n = 50)	Hematoma expansion		p value
		No (n = 36)	Yes (n = 14)	
Baseline NCCT shape features				
Irregular shape, n (%)	40 (80.0)	26 (72.2)	14 (100)	0.045
Island sign, n (%)	5 (10.0)	2 (5.6)	3 (21.4)	0.126
Satellite sign, n (%)	5 (10.0)	4 (11.1)	1 (7.1)	1.000
Baseline NCCT density features				
Fluid level, n (%)	4 (8.0)	2 (5.6)	2 (14.3)	0.310
Blend sign, n (%)	8 (16.0)	4 (11.1)	4 (28.6)	0.197
Black hole sign, n (%)	5 (10.0)	1 (2.8)	4 (28.6)	0.018
Hypodensity, n (%)	24 (48.0)	10 (27.8)	14 (100)	< 0.001
Swirl sign, n (%)	5 (10.0)	1 (2.8)	4 (28.6)	0.018
Heterogeneous density, n (%)	4 (8.0)	1 (2.8)	3 (21.4)	0.061

NCCT: noncontrast computed tomography.

DISCUSSION

In our study, an HU value of 64.2 or less in the ROC analysis proved to be the optimal cut-off point for predicting hematoma expansion in baseline NCCT patients diagnosed with ICH. This HU value was defined for the first time and provides a prognostic imaging marker in the NCCT for rapid identification of patients at risk of hematoma expansion who may benefit from specific therapeutic interventions.

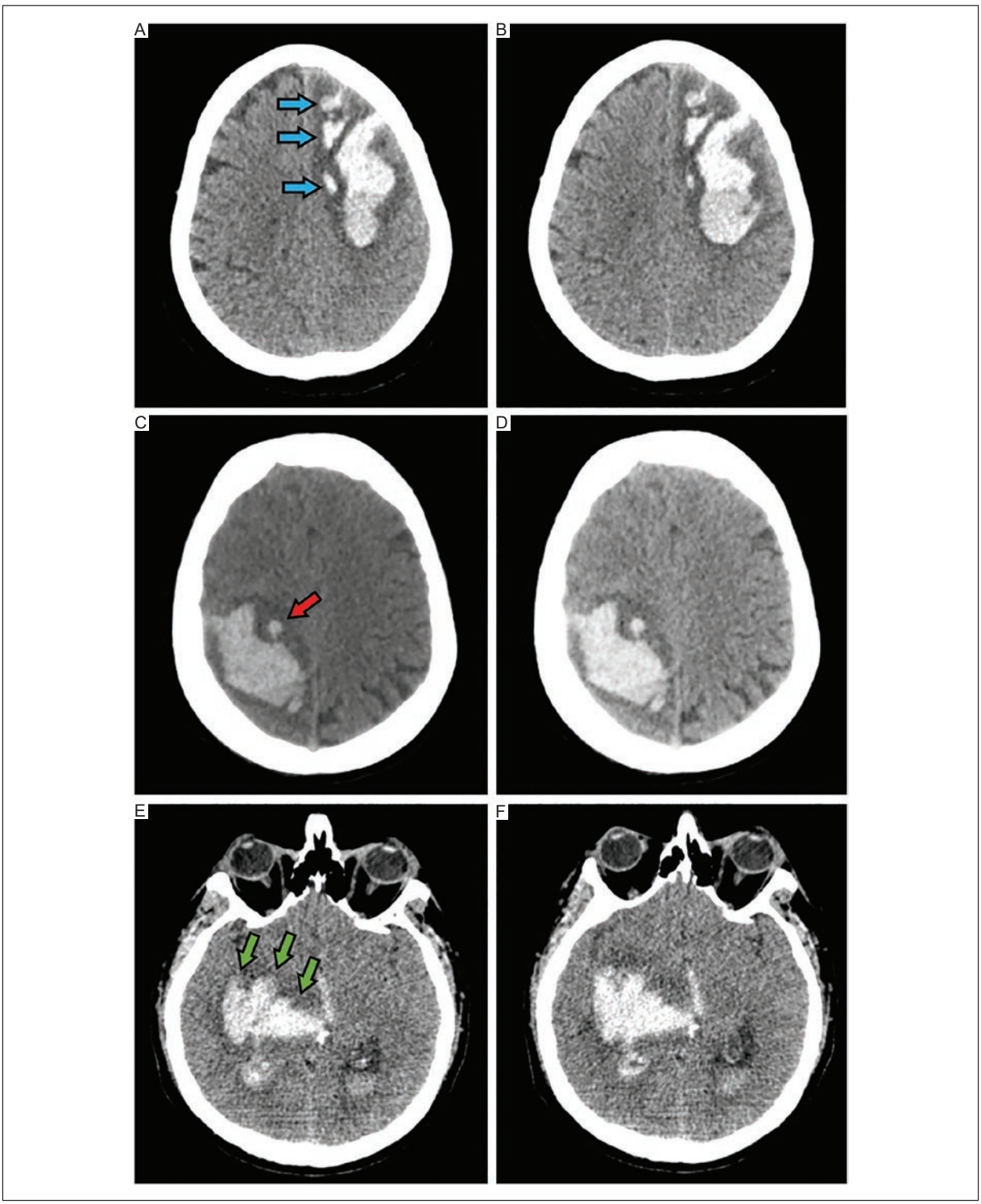


Figure 4. Hematoma shape features. A and B: axial NCCT of a 77-year-old woman with thrombocytopenia, ICH score 2. **A:** baseline NCCT, 6 hours after symptom onset, showing left frontal hematoma with Island sign (arrows), an initial volume of 47.6 mL, and a mean attenuation coefficient of 61.7 HU. **B:** follow-up NCCT 35 hours after baseline NCCT shows hematoma expansion with a volume of 83.5 mL. **C and D:** axial NCCT of a 71-year-old hypertensive and diabetic woman, ICH score 1. **C:** baseline NCCT, 8 hours after symptom onset, showing a right frontal hematoma with satellite sign (arrow), an initial volume of 36.6 mL, and a mean attenuation coefficient of 80.6 HU. **D:** follow-up NCCT 26 hours after baseline NCCT showing hematoma with a volume of 24.9 mL. **E and F:** axial NCCT of a 46-year-old man with thrombocytopenia, ICH score 4. **E:** baseline NCCT, 5 hours after symptom onset, showing a right thalamic hematoma with irregular hematoma shape (arrow), an initial volume of 26.0 mL, and a mean attenuation coefficient of 59.0 HU. **F:** follow-up NCCT 18 hours after baseline NCCT showing expansion of the hematoma with a volume of 38.8 mL.

NCCT: noncontrast CT; HU: Hounsfield units; ICH: intracerebral hemorrhage; mL: milliliters.

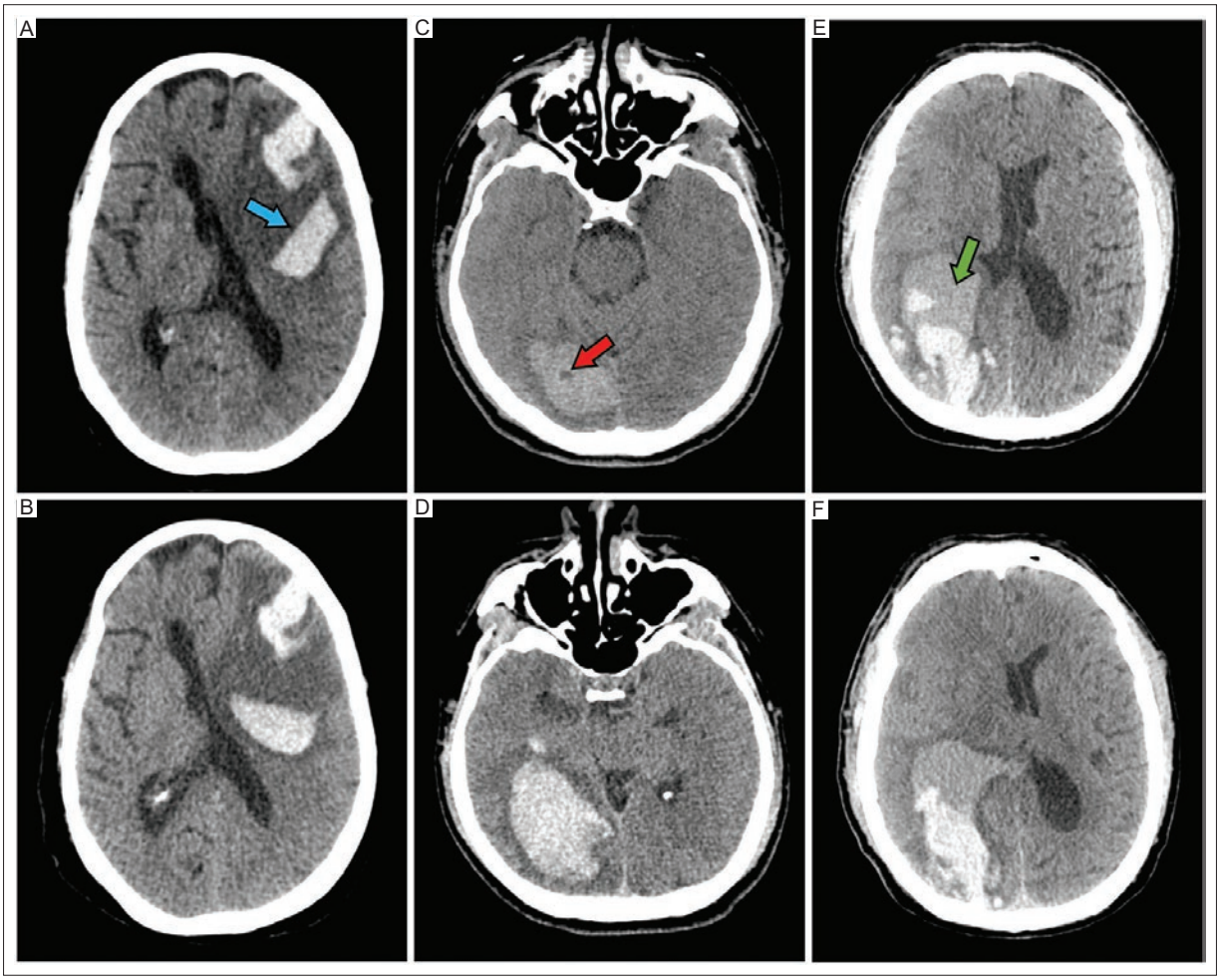


Figure 5. Hematoma density features. A and B: Axial NCCT of a 76-year-old hypertensive and diabetic woman, ICH score 2. **A:** baseline NCCT, 6 hours after symptom onset, showing left frontal hematoma with fluid level (arrow), an initial volume of 45.7 mL and a mean attenuation coefficient of 59.0 HU. **B:** follow-up NCCT 25 hours after baseline NCCT showing hematoma expansion with volume of 54.7 mL. **C and D:** axial cranial NCCT of a 37-year-old man treated with oral anticoagulants for prosthetic heart valve: Lobar ICH, score 1. **C:** baseline NCCT 7 hours after symptom onset, showing a right occipital hematoma with the black hole sign (arrow), an initial volume of 39.5 mL, and a mean attenuation coefficient of 61.0 HU. **D:** follow-up NCCT at 24 hours after baseline NCCT showing hematoma expansion with a volume of 80.1 mL. **E and F:** axial cranial NCCT of a 61-year-old hypertensive and diabetic woman, ICH scale 2. **E:** baseline NCCT, 4 hours after symptom onset, showing a right parietal hematoma with the blend sign (arrow), an initial volume of 63.2 mL, and a mean attenuation coefficient of 58.0 HU. **F:** follow-up NCCT 71 hours after baseline NCCT shows hematoma expansion with a volume of 75.6 mL.

NCCT: noncontrast CT; HU: Hounsfield units; ICH: intracerebral hemorrhage; mL: milliliters.

The incidence of hematoma expansion varies from 13 to 40%[3,5,6], and an inverse relationship between HU and the risk of hematoma expansion has been reported[3,5,7]. In the study by Kim et al.[7], in 232 patients with ICH, hematoma expansion was detected in 80 (34.5%). The mean HU showed significantly lower values in patients with hematoma expansion (56.8 ± 3.0 HU) compared with cases without expansion (58.5 ± 3.3 HU) ($p < 0.01$). The elapsed time between symptom onset and baseline NCCT was 1.9 hours (range, 1.2-4.9) compared with 2.2 hours (range, 1.3-4.5), respectively. Jeong et al.[3], in a study of 89 patients with ICH, found hematoma expansion in 33 (37.1%) cases. The mean HU at baseline NCCT showed a lower value in patients with hematoma expansion (55.7 ± 2.9 HU) compared with cases without expansion (58.6 ± 3.1 HU) ($p < 0.01$). The time between symptom onset and baseline NCCT averaged 2.9 hours in both groups. In our study of 50 patients with ICH, hematoma expansion was present in 14 (28.0%). The mean HU at baseline NCCT showed significantly lower values in patients with hematoma expansion (61.1 ± 2.8 HU) compared with patients without expansion (69.2 ± 5.5 HU) ($p < 0.001$). The mean time between symptom onset and baseline NCCT was 6.6 ± 1.40 and 6.3 ± 1.22

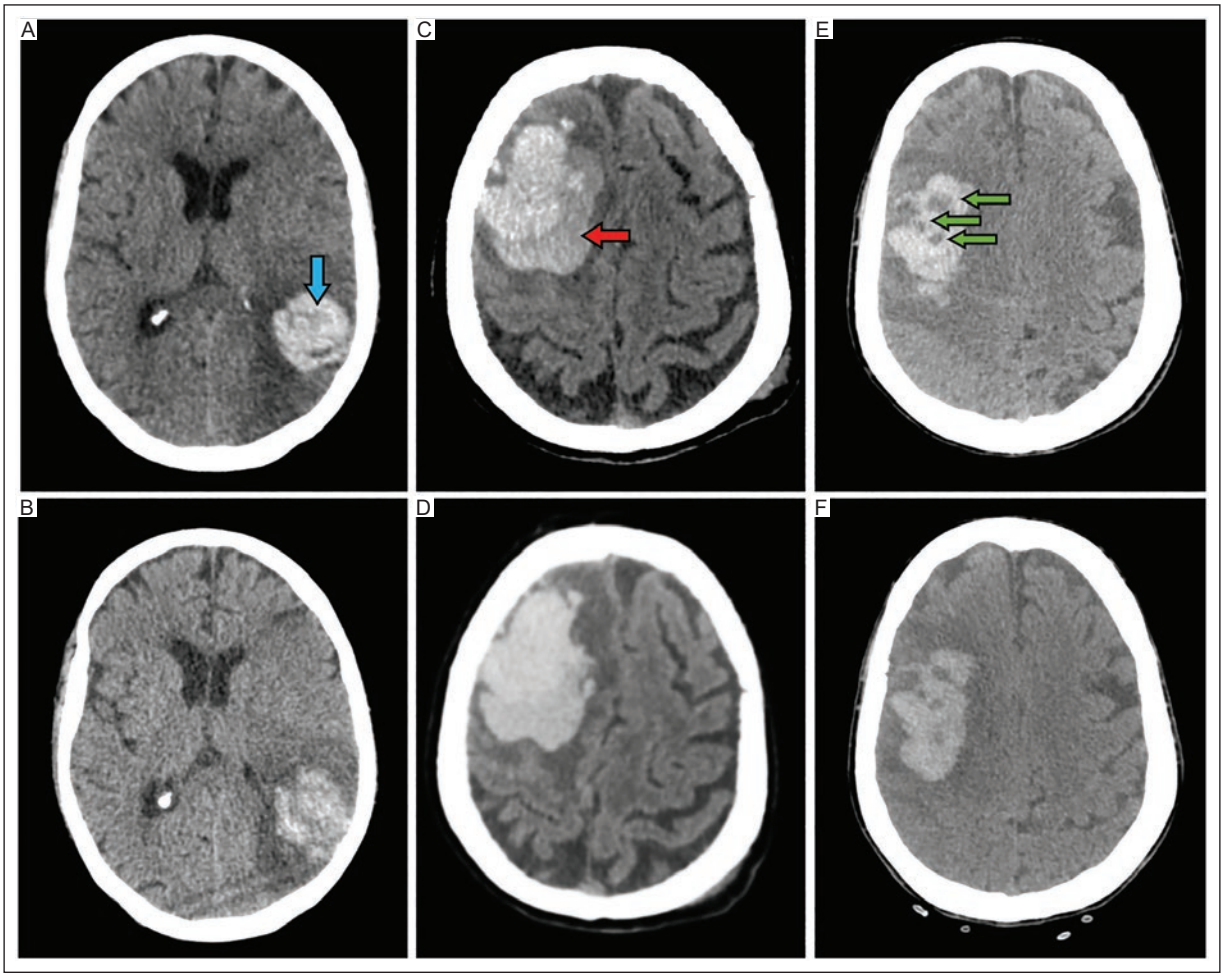


Figure 6. Hematoma density features. A and B: axial cranial NCCT of a 52-year-old hypertensive man, ICH scale 2. **A:** baseline NCCT, 7 hours after symptom onset, showing left parietal hematoma with swirl sign (arrow), an initial volume of 30.4 mL, and mean attenuation coefficient of 57.7 HU. **B:** follow-up NCCT at 30 hours after baseline NCCT showing hematoma expansion with a volume of 38.5 mL. **C and D:** axial cranial NCCT of a 76-year-old hypertensive and diabetic woman, ICH score 2. **C:** baseline NCCT, 6 hours after symptom onset, showing right frontal hematoma with hypodensity (arrow), an initial volume of 45.7 mL and a mean attenuation coefficient of 59.0 HU. **D:** follow-up NCCT 25 hours after baseline NCCT showing hematoma expansion with a volume of 54.7 mL. **E and F:** axial cranial NCCT of a 72-year-old woman, hypertensive ICH scale 1. **E:** axial baseline cranial NCCT four hours after symptom onset. It shows a right frontal hematoma with heterogeneous density (arrows), an initial volume of 33.9 mL, and a mean attenuation coefficient of 67.8 HU. **F:** follow-up NCCT 7 hours after baseline NCCT showing hematoma expansion with a volume of 40.2 mL.

NCCT: noncontrast CT; HU: Hounsfield units; ICH: intracerebral hemorrhage; mL: milliliters.

hours, respectively. In our study, the higher mean HU value compared with previous reports[5,7] might be related to the longer time interval between the onset of symptoms of ICH and baseline NCCT in both groups; a longer period of coagulation contraction with increased hematocrit might be reflected in increased HU in both groups. Then, the proposed value of 64.2 HU or less might be applicable to predict hematoma expansion if the time between symptom onset and baseline NCCT is comparable to our study population.

Shape and density features at baseline NCCT have a variable association with the risk of hematoma expansion in patients with ICH[3,10,11]. In a meta-analysis including 23 studies, hematoma expansion was reported in 7% to 40% of 10,363 patients with ICH patients[10]. Shape characteristics (island sign and irregular) showed differences in sensitivity (32 to 68%) and specificity (47 to 92%) for predicting hematoma expansion. On the other hand, density features (black hole sign, hypodensity, heterogeneous density, and blend sign) showed differences in sensitivity (28 to 63%) and specificity (65 to 89%)[10]. In the study by Boulouis et al.[1] of 784 patients with ICH, hypodensity was observed in 86 (52.8%) of 163 patients with hematoma expansion. In contrast,

this finding was present in 136 (21.9%) of 621 patients without hematoma expansion ($p < 0.001$). In our study, shape (irregularity) and density (black hole, swirl, and hypodensity) in baseline NCCT showed no differences in the final multivariate model between patients with and without hematoma expansion. Previous studies have found a variable association between shape, density, and volume in NCCT at baseline and increased risk of hematoma expansion in patients with ICH[3,10].

The relationship between the initial volume and risk of expansion is maximal when it is approximately 75 mL[3]. In our study, no difference in mean initial volume was found between patients with and without hematoma expansion (27.22 ± 16.54 mL and 25.75 ± 18.67 mL, respectively). A volume greater than 25 mL is associated with a higher risk of hematoma expansion because the larger volume increases the shear effect of the vessels, causing expansion of the hematoma[11].

An inverse relationship between hemoglobin, hematocrit, and platelet count and the risk of hematoma expansion in patients with ICH has been reported[5,7]. Jeong et al.[5], in a study of 89 patients with ICH, reported lower hematocrit values (39.4 ± 7.2 vs. 43.7 ± 5.2) ($p < 0.01$) and platelet count (191 ± 54 x 10^9/L vs. 216 ± 54 × 10^9/L) ($p = 0.04$) in patients with and without hematoma expansion, respectively. In a study by Kim et al.[7] that included 232 patients with ICH, lower values were found for hemoglobin (13.3 ± 2.4 g/dL vs. 14.2 ± 1.8 g/dL) ($p < 0.01$), hematocrit (40.1 ± 6.6 vs. 42.6 ± 4.9 ($p < 0.01$), and platelets (210.5 ± 59 × 10^9/L vs. 216.4 ± 62.4 × 10^9/L) ($p = 0.49$) in patients with and without hematoma expansion, respectively. In our study, the platelet count was significantly lower with expansion (185.43 ± 97.82 × 10^9/L) compared to without hematoma expansion (260.47 ± 72.79 × 10^9/L) ($p = 0.016$). No correlation was found between hemoglobin levels and hematoma expansion. The mechanisms of the inverse relationship between hemoglobin, hematocrit, platelet count, and the risk of hematoma expansion are unclear.

The strengths of the study are the prospective cohort design and the performance of NCCT examinations at baseline and follow-up in all patients. The limitations are related to the small sample size in a single center. On the other hand, measurements of the HU were performed with manual volumetry, which is less accurate than semi-automated techniques. Interobserver agreement was not assessed.

CONCLUSION

The optimal HU value to predict hematoma expansion was defined on the baseline NCCT in patients diagnosed with ICH. HU may be a useful image marker to guide therapeutic decisions such as hemostatic therapy or drainage in patients at risk of hematoma expansion. Validation of the optimal HU value for predicting hematoma expansion and a definition of its clinical utility in a large cohort of patients with ICH are needed.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of Individuals. This study was conducted in compliance with the Declaration of Helsinki (1964) and its subsequent amendments.

Confidentiality of Data. The authors declare they followed their center's protocol for sharing patient data.

Right to privacy and informed consent. Informed consent was not required for this observational study of information collected during routine clinical care.

REFERENCES

1. Boulouis G, Morotti A, Brouwers HB, Charidimou A, Jessel MJ, Auriel E, et al. Association Between Hypodensities Detected by Computed Tomography and Hematoma Expansion in Patients with Intracerebral Hemorrhage. JAMA Neurol. 2016;73(8):961-968. doi:10.1001/jamaneurol.2016.1218.
2. Zimmerman RD, Maldjian JA, Brun NC, Horvath B, Skolnick BE. Radiologic estimation of hematoma volume in intracerebral hemorrhage trial by CT scan. AJNR Am J Neuroradiol. 2006;27(3):666-670.
3. Morotti A, Boulouis G, Dowlatshahi D, Li Q, Shamy M, Salman RA, et al. Intracerebral haemorrhage expansion: definitions, predictors, and prevention. Lancet Neurol. 2023;22(2):159-171. doi: 10.1016/S1474-4422(22)00338-6.

4. Xu M, Lin J, Lei C, Liu J, Yuan R, Tan G, et al. High Level of Serum Myoglobin in Human Intracerebral Hemorrhage: Implications for Large Hematoma Volume and Growth. J Stroke Cerebrovasc Dis. 2016;25(7):1582-1589. doi:10.1016/j.jstrokecerebrovasdis.2016.02.005.
5. Jeong HG, Bang JS, Kim BJ, Bae HJ, Han MK. Hematoma Hounsfield units and expansion of intracerebral hemorrhage: A potential marker of hemostatic clot contraction. Int J Stroke. 2021;16(2):163-171. doi:10.1177/1747493019895703.
6. Brouwers HB, Greenberg SM. Hematoma expansion following acute intracerebral hemorrhage. Cerebrovasc Dis. 2013;35(3):195-201. doi:10.1159/000346599.
7. Kim YS, Jeong HG, Chae HY, Kim BJ, Kang J, Kim JY, et al. Mediation effects of mean Hounsfield unit on relationship between hemoglobin and expansion of intracerebral hemorrhage. Sci Rep. 2021;11(1):17236. doi:10.1038/s41598-021-96790-x.
8. Schlunk F, Greenberg SM. The Pathophysiology of Intracerebral Hemorrhage Formation and Expansion. Transl Stroke Res. 2015;6(4):257-263. doi:10.1007/s12975-015-0410-1.
9. Al-Shahi Salman R, Frantzias J, Lee RJ, Lyden PD, Battey TWK, Ayres AM, et al. Absolute risk and predictors of the growth of acute spontaneous intracerebral haemorrhage: a systematic review and meta-analysis of individual patient data. Lancet Neurol. 2018;17(10):885-894. doi:10.1016/S1474-4422(18)30253-9. Erratum in: Lancet Neurol. 2018 Sep 19.
10. Arba F, Rinaldi C, Boulouis G, Fainardi E, Charidimou A, Morotti A. Noncontrast Computed Tomography Markers of Cerebral Hemorrhage Expansion: Diagnostic Accuracy Meta-Analysis [published online ahead of print, 2021 Nov 29]. Int J Stroke. 2021;17474930211061639. doi:10.1177/17474930211061639.
11. LoPresti MA, Bruce SS, Camacho E, Kunchala S, Dubois BG, Bruce E, et al. Hematoma volume as the major determinant of outcomes after intracerebral hemorrhage. J Neurol Sci. 2014;345(1-2):3-7. doi:10.1016/j.jns.2014.06.057.
12. Hemphill JC 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. Stroke. 2001;32(4):891-897. doi:10.1161/01.str.32.4.891.