Predictive value of imaging manifestations of supratentorial hemorrhage in hematoma enlargement and clinical prognosis

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Abstract

Introduction: Intracerebral hemorrhage (ICH) is an important cause of death and disability. This study aimed to explore the imaging indicators identifying hematoma expansion in primary ICH and to provide a basis for its clinical treatment.
Material and methods: Hematoma expansion was evaluated by plain computed tomography (CT) scan and multi-detector-row CT angiography (MDCTA).
Results: This study included a total of 203 patients with intracerebral hemorrhage. The size of the hematoma at the time of admission was 32.5–92.3 ml (mean: 45.5 ml). Original or reconstructed MDCTA images with contrast extravasation were available in 35 (17.2%) cases. Patients were divided into two groups based on whether or not hematoma expansion had occurred: the hematoma expansion group (n = 87) and the no hematoma expansion group (n = 116). Percentages of patients with spot signs in the two groups were 37.93% and 3.45%, respectively, and percentages of those with spot sign ± blend sign ± black hole sign ± island sign (%) were 48.30% and 1.72%, respectively, with statistically significant differences. The sensitivity, specificity, and positive and negative predictive values of hematoma enlargement were 37.93%, 98.27%, and 94.29% and 67.86%, respectively. The sensitivity, specificity, and positive and negative predictive values of blend density sign ± irregular sign in predicting hematoma enlargement in ICH patients were 97.7%, 76.7%, and 75.9% and 97.8%, respectively.
Conclusions: Blend density sign ± irregular sign can be used as substitute signs. The more irregular and uneven density the hematoma, the more likely it is that the hematoma will be enlarged.

Key words: cerebral angiography, cerebral hemorrhage, sensitivity and specificity, hematoma, computed tomography angiography, tomography, X-ray computed.

Introduction

Primary intracerebral hemorrhage (ICH) is an important cause of death and disability. The incidence of intracerebral hemorrhage in the Asian stroke population has been reported to be in the range 20–30%, which was significantly higher, even twice as high, as that reported from western countries [1]. This difference in incidence may be related to the distribution of risk factors such as genes, environment, and hypertension [2, 3]. The neurological function often deteriorates rapidly within a few hours of onset of ICH [4]; therefore, it is vital to rapidly diagnose and treat this condition when it occurs.

Hematoma expansion has been considered to be one of the most important determinants of neurological deterioration and poor clinical outcomes in the early stage of primary ICH [5]. After ICH, secondary injury occurs as a result of expansion of the hematoma and peri-hematoma edema [6]. Hematoma expansion is an important risk factor involved in the deterioration of neurological function and poor prognosis in the early stage of ICH [7, 8].

The aim of the present study was to retrospectively investigate the signs of contrast extravasation (spot sign) and other CT computed tomography angiography (CTA) A image signs in patients with ICH obtained during the hyperacute period of primary ICH and their relationship with the location, size, morphology, and clinical prognosis of hematomas. We hope that the results can help us explore the imaging indicators of hematoma expansion in primary ICH and provide a basis for clinical monitoring of disease changes and strengthening antihypertensive therapy or timely selection of surgical intervention.

Material and methods

Study population and design

This study retrospectively analyzed data of patients with hemorrhagic stroke who had been treated at the Department of Neurology and Neurosurgery, Pudong New Area People's Hospital in Shanghai, from January 2017 to December 2019.

The inclusion criteria were as follows: (1) patients who were aged 18–80 years, (2) those who arrived at the hospital within 6 h of onset; and (3) those with primary intracerebral hemorrhage confirmed by emergency computed tomography (CT) examination.

The exclusion criteria were as follows: (1) patients with deep coma (Glasgow coma score [GCS] of 3–5 points); (2) those who were allergic to contrast medium; (3) patients with previous thyroid disease or renal dysfunction; (4) those with congenital or acquired coagulation dysfunction; (5) those who did not complete CT plain scan and MDCTA.

This study was approved by the Ethics Committee of the Pudong New Area People's Hospital in Shanghai. As this was a retrospective study, informed consent was waived.

Imaging examination

Whole-brain CT scan was performed at the emergency admission, and further CTA was performed after hemorrhage was confirmed. A 64-row CT scanner (Philips, the Netherlands) was used for examination. Patients received a 70 ml ioversol dose administered intravenously through the median elbow vein using a high-pressure syringe at a rate of 5 ml/s. CTA parameters were set to 120 kV and 300 mA. Imaging operations were completed by a technician with more than 5 years of working experience. All the images were uploaded to the Neusoft picture archiving and communication system for analysis. The obtained imaging results were observed and evaluated by two experienced neuroradiologists.

Clinical indicators and definition

Clinical data of the patients, including demographics, medical history at the time of admission, and clinical features, were collected for use in this study. Demographic characteristics included gender and age; medical history included history of drinking, hypertension, and diabetes. The clinical characteristics included systolic blood pressure, diastolic blood pressure, GCS [9, 10], and the National Institutes of Health Stroke Scale (NIHSS) score that were obtained at the time of admission.

According to the standard proposed by Delgado Almandoz *et al*. [11], hematoma expansion is defined as an increase in the size of the hematoma in ICH patients on subsequent CT scans by > 12.5 ml or > 33% compared with the first CT, when the first CT scan is within 6 h of ICH onset and the second CT scan is performed within 24 h after the first CT. The volume of the hematoma was evaluated using the method of three-dimensional drawing [12], which was especially suitable to measure irregular hematoma.

On imaging, when a black hole (low-density area) in the hematoma was completely surrounded by an adjacent high-density hematoma, and satisfied the following criteria – (1) the shape was different, but not connected with adjacent brain tissues; (2) there was a clear boundary; (3) and CT values of the two different density areas in the hematoma differed by at least 28 HU – it was then regarded as a black hole sign [13, 14].

On imaging, the presence of relatively low-density areas and adjacent high-density areas in the same hematoma was defined as a blend sign [15], provided the following conditions were satisfied: (1) there was an obvious boundary between the low- and high-density areas that could be recognized by the naked eye, (2) the CT values of the two different density areas in the hematoma differed by at least 18 HU, and (3) the low-density area was not completely enclosed by the high-density area. A blend sign was considered when all the above criteria were simultaneously met.

The black hole sign and blend sign were identified on plain CT scan images, and contrast medium extravasation signs and spot signs were identified on original or reconstructed MDCTA images, and spot sign scoring was completed.

Two CTA scans were performed for each ICH patient, including a CTA phase and a delayed phase (5 min after the CTA phase). The region of interest (ROI) was set with a diameter of 10 mm, and the CT value was calculated. When the CT value in the ROI at the delayed phase was more than 10% higher than that in the CTA phase, this phenomenon was defined as a leakage sign [16].

An enhanced lesion in the hematoma on the original CTA image was referred to as the spot sign [11]. According to the spot sign criteria proposed by Delgado *et al.* in 2009, a spot sign was considered to be present provided: 1) there was ≥ 1 enhanced lesion with concentrated contrast medium in the extravasation area of the intracranial hematoma; 2) compared with its density, the attenuation of the peripheral hematoma was greater than 120 HU, 3) the CTA spot sign should be separated from the blood vessels in the hematoma, and 4) the spot sign should be located within the intracranial hematoma.

CT re-examination was then performed at 24 h, 2 days, and after 90 days. NIHSS scoring, 90-day quality of life, Barthel index (BI) [17] (range: 0 [severe disability] to 100 [no disability]), and mRS scoring [18–22] (range: 0 [no symptoms] to 5 [severe disability]) were performed at the time of admission and at 24 h, 7 days, and 14 days.

Mortality was observed during hospitalization, and patients who survived were followed up to observe their quality of life at 6 months after surgery.

The patients were categorized into one of five grades based on their activities of daily living (ADL) score [23]: grade 1, complete recovery of the family's ability to perform daily life activity; grade 2, the ability to perform daily life activities independently and partial recovery of social life; grade 3, some assistance was needed for daily life activities; grade 4, the patient retained consciousness, but assistance was needed for all daily life activities, and grade 5, survival in the vegetative state. Grades 1, 2, and 3 were good effects while grades 4 and 5 were bad effects.

Treatment

According to the Chinese guidelines for the diagnosis and treatment of ICH (2014), craniotomy or minimally invasive surgery was performed to surgically remove the supratentorial hematoma in patients with lobar hemorrhage of > 30 ml and within 1 cm of the cortical surface. Patients who presented with supratentorial ICH with a hematoma volume within the range 20–40 ml, a GCS score of ≥ 9, and were within 72 h of onset could be treated with minimally invasive surgery with or without liquidation by thrombolytic drugs for drainage of the hematoma after strict selection. In cases where patients had severe cerebral hemorrhage exceeding 40 ml, in whom the disturbance of consciousness worsened due to the space-occupying effect of the hematoma, craniotomy was performed to remove the hematoma.

Statistical analysIs

Statistical analysis was performed using SPSS software version 25.0 (IBM, Armonk, NY, USA). Continuous variables that conformed to normal distribution were presented as the mean ± SD, and continuous variables that did not conform to the normal distribution were represented as the median (range or interquartile [IQR] range). Classification variables were presented as *n* (%). For continuous variables with normal distribution, the *t* test and analysis of variance (ANOVA) were used, and non-normally distributed continuous variables were tested by the Mann-Whitney *U* test or the Kruskal-Wallis test. The χ^2 test or Fisher's exact test was used for statistical analysis of categorical variables.

Results

We analyzed 203 patients with ICH in the present study, of whom 87 had hematoma expansion while 116 had no hematoma expansion. The average size of the hematoma at the first admission was 32.5–92.3 ml (mean: 45.5 ml). A total of 35 (17.2%) cases had contrast medium extravasation signs on original or reconstructed MDCTA images, and spot sign scoring was performed. The relevant imaging manifestations were recorded, and a hematoma volume > 33% or 12.5 ml compared with the first scan image as defined previously was considered as a hematoma expansion. Table I shows the baseline data of 203 cases of ICH in the hematoma expansion and no expansion groups, and Table II and Supplementary Figures 1–4 present the clinical and imaging data.

A total of 69 cases received skull drilling for hematoma removal. The drainage volume ranged from 20 to 92 ml with an average of 46.5 ml, accounting for 40–70% of the hematomas. The postoperative NIHSS score was 3–24 points, with an average of 8.5 points. Of these, 4 cases underwent craniotomy after skull drilling and drainage due to hematoma expansion.

Table III shows that the sensitivity, specificity, and positive and negative predictive values of

Table I. Baseline data of 203 cases of cerebral hemorrhage in the two groups

Clinical baseline data	Hematoma expansion group (*n* = 87)	No hematoma expansion group (*n* = 116)	*P*-value
Age [years]	59.25 ± 9.46	56.17 ± 8.59	0.175
Male (%)	55.17 (48/87)	58.62 (68/116)	0.505
Hypertension (%)	83.90 (73/87)	81.90 (95/116)	0.536
Atrial fibrillation (%)	9.20 (8/87)	8.33 (10/116)	0.578
Diabetes (%)	12.64 (11/87)	9.48 (11/116)	0.732
Stroke side (left/right)	45/42	61/55	0.425
Time of onset [h]	2.30 ±1.46	2.15 ±1.63	0.233

There was no significant difference in the baseline data of patients with cerebral hemorrhage between the two groups (p > 0.05).

Table II. Clinical and imaging data of 203 cases of cerebral hemorrhage in the two groups

Items	Hematoma expansion group (*n* = 87)	No hematoma expansion group (*n* = 116)	*P*-value
Baseline NIHSS	11.53 ±4.82	10.98 ±4.11	0.296
24-h NIHSS	17.74 ±4.36	12.08 ±4.73	0.008
7-day NIHSS	15.05 ±4.23	5.68 ±4.96	< 0.001
CTA spot sign (%)	37.93 (33/87)	3.45 (2/116)	< 0.001
Blend sign (%)	11.50 (10/87)	2.59 (3/116)	< 0.001
Black hole sign (%)	13.79 (12/87)	3.45 (4/116)	< 0.001
Island sign	10.34 (9/87)	2.59 (2/116)	< 0.001
Spot sign ± blend sign ± black hole sign ± island sign (%)	48.30 (42/87)	1.72 (6/116)	< 0.001
Irregular hematoma sign (%)	87.36 (76/87)	21.55 (25/116)	< 0.001
Blend density sign (%)	93.10 (81/87)	19.83 (23/116)	< 0.001
Irregular hematoma sign ± blend density sign (%)	97.7 (85/87)	23.28 (27/116)	< 0.001
Mortality rate (%)	16.09 (14/87)	6.90 (8/116)	0.005
90-day mRS (0 or 1) (%)	49.32 (36/73)	66.67 (72/108)	0.009
90-day BI (≥ 90) (%)	52.05 (38/73)	68.52 74/108)	0.006
Good survival at 6 months (grade 1, 2, and 3 of ADL scoring)	54.80 (40/73)	71.30 (77/108)	0.009

NIHSS – National Institutes of Health Stroke Scale, CTA – CT angiography, mRS – modified Rankin scale, BI – Barthel index, ADL – activities of daily living. There was no significant difference in the baseline NIHSS score between the two groups (p > 0.05), but the 24-h and 7-day NIHSS scores were both significantly better in the no hematoma expansion group than in the hematoma expansion group (p < 0.01).

Table III. ROC prediction of each variable

Variable	Sensitivity	Specificity	PPV	NPV
Hematoma expansion	37.93%	98.27%	94.29%	67.86%
Blend density sign ± Irregular sign	97.7%	76.7%	75.9%	97.8%

hematoma expansion were 37.93%, 98.27%, and 94.29% and 67.86%, respectively. The sensitivity, specificity, and positive and negative predictive values of blend density signs ± irregular signs in predicting hematoma expansion in ICH patients were 97.7%, 76.7%, and 75.9% and 97.8%, respectively.

Five and seventeen patients in the surgical and non-surgical treatment groups died after surgery during hospitalization (mortality rate: 10.84%). The causes of death were brainstem failure caused by hematoma expansion or rebleeding in 12 cases, acute renal failure in 3 cases, and multiple organ failure in 7 cases. At the 6-month post-surgical follow-up, 54 patients survived well after surgery in the hematoma expansion group (good rate, 78.3%), and 2 of the 18 in the no surgery hematoma expansion group showed good survival (good rate: 11.11%). The 181 patients who survived were followed up with postoperative CT re-examination. The results of the postoperative scan revealed a gradual decrease in hematoma size or disappearance of most of the hematoma, until finally encephalomalacia foci remained.

Discussion

Hematoma expansion is a very common feature of ICH and occurs in 40% of patients with ICH, and it is considered an independent predictor of disease deterioration and poor prognosis [7]. Liu *et al*. [24] and Wu *et al*. [25] attempted to predict hematoma expansion in patients with ICH using support vector machine method with good results. Other studies have used imaging findings such as presence of a satellite sign or spot sign on CT scans to predict hematoma expansion [26]. Currently, however, no unified diagnostic standard exists, and diagnosis of ICH primarily depends on CTA and CT examination. We retrospectively studied CT and MDCTA findings of 203 patients and compared various imaging findings between two groups (one with hematoma expansion and one without hematoma expansion). In our study, the results indicated that blend density ± irregular sign could be used as substitute signs on CT and CTA scans to predict hematoma expansion.

Recent studies have confirmed that some CTA and CT manifestations are known to be associated with hematoma expansion, such as spot sign, leakage sign, blend sign, black hole sign and island sign [26]. These imaging manifestations provide a more effective method to diagnose high-risk patients with ICH with hematoma expansion. Therefore, this study aimed to analyze the potential correlation between the manifestations of hematoma in CTA and CT scans and early hematoma expansion in patients with ICH, so that a timely and effective clinical intervention may be carried out for ICH patients with hematoma expansion, consequently reducing their mortality rate and improving the prognosis.

The present study showed that spot sign, blend sign, black hole sign, and island sign reflect the heterogeneity of hematomas, and can predict the expansion of some types of hematomas. Together, the spot sign, blend sign, black hole sign, and island sign show high specificity, but any of these signs exhibit low individual sensitivity. CTA examination in patients with ICH at an early stage was poorly operable, and was unsuitable for patients with obviously impaired renal function. In addition, the imaging standards of point sign, blend sign, black hole sign, and island sign were complicated and difficult for clinicians to grasp and operate quickly. We recommended blend density sign and/or the irregular sign as substitute signs. The sensitivity, specificity, and the positive and negative predictive values of blend density sign and/or irregular sign for predicting hematoma expansion in ICH patients were 97.7%, 76.7%, and 75.9% and 97.8%, respectively. Although the specificity and positive predictive value of these signs were slightly lower, their sensitivity and negative predictive values were relatively high. There was a statistically significant difference between predicting hematoma expansion and no expansion, and the evaluation indicator was simple. The maneuverability was strong. Preliminary studies have demonstrated that the more irregular and uneven the hematoma, the more it is likely that hematoma expansion will occur.

This study has some limitations. First, it is a single-center study that requires external validation of our results. Second, the study had a small sample size. Future multicenter studies with a larger sample size should be conducted on the basis of our study findings.

For the 69 patients who underwent minimally invasive surgery or craniotomy, 5 and 17 patients in the surgery and no surgery groups died during hospitalization (mortality rate: 10.84%). The follow-up conducted 6 months post-surgically showed that 54 and 2 patients survived well in the hematoma expansion surgery and no surgery group (good outcome rates, 78.3% and 11.11%, respectively). Preliminary studies showed that minimally invasive treatment affected the precise treatment of hematomas in patients with ICH [27].

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Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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