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ORIGINAL ARTICLE

Perihematomal Perfusion Typing and Spot Sign of Acute Intracerebral Hemorrhage with Multimode Computed Tomography: A Preliminary Study

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Key words: intracerebral hemorrhage; computed tomography perfusion; computed tomography angiography

Objective To explore the perihematomal perfusion typing and spot sign on computed tomography angiography (CTA) source images in order to assist in individualizing therapeutic decisions for patients with intracerebral hemorrhage by possibly forecasting perihematomal ischemia and hematoma enlargement.

Methods We examined 58 patients with spontaneous intracerebral hemorrhage by computed tomography perfusion and CTA within 6 hours after symptom onset. Hematoma volumes were determined from non-contrast CT images and compared between first and second CT images. The perfusion of hematoma region and perihematoma region was evaluated for presence or absence of the perihematomal penumbra. Three kinds of perihematoma perfusion typing were defined according to the perfusion of hematoma region and perihematoma region. CTA source images was reviewed to make sure presence or absence of the spot sign.

Results Finally, 53 patients (34 males, 19 females) were enrolled in our study according to exclusion criteria. Finally, 21 patients were classified into the normal group, 23 patients were classified into the mild group, and 9 patients were classified into the severe group. There were significant differences in hematoma size between the presence and absence of the perihematomal penumbra group ($P < 0.05$). Thirteen (24.5%) patients presented with spot sign. Hematoma expansion occurred in 15 (28.3%) patients on follow-up. In which 12 patients were with spot sign. Sensitivity, specificity, positive predictive value, and negative predictive value for expansion were 80.0%, 97.4%, 92.3%, and 92.5%, respectively.

Conclusion In acute intracerebral hemorrhage patients, the perihematoma perfusion typing and CTA spot sign provide more radiological information that might assist in individualizing therapeutic decisions for patients by possibly forecasting perihematomal ischemia and hematoma enlargement.

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INTRACEREBRAL hemorrhage (ICH) accounts for 10% to 15% of cerebrovascular diseases. It is associated with higher morbidity and mortality than other stroke subtypes.¹ But in contrast to the many therapeutic advances that have been developed for ischemic stroke and subarachnoid hemorrhage in recent years, there remains a lack of effective treatment for ICH.² Secondary brain injury and hematoma enlargement contribute significantly to morbidity and mortality after ICH. Perihematoma penumbra is one of the most important types of secondary brain injury after ICH.³ Elevated blood pressure (BP) may cause hematoma enlargement in acute ICH. On the other hand, there may be areas of penumbra adjacent to a hematoma, and reduction of BP has been assumed to promote further ischemia. Elevated BP can also be a protective response to preserve cerebral perfusion.⁴ So there are two questions for us to choose the best treatment for every patient. First is how to set an appropriate target BP? Second, whether we should use hemostasis or improve microcirculation treatment for the patients? Maybe computed tomography perfusion (CTP) and computed tomography angiography (CTA) including CTA source images (CTA-SI) in the ICH patients can help us to answer these questions. The aim of our study was to explore the perihematoma perfusion typing and spot sign on CTA-SI in order to assist in individualizing therapeutic decisions for ICH patients by possibly forecasting perihematoma ischemia and hematoma enlargement.

PATIENTS AND METHODS

Patients

The study was approved by the Committee of the Beijing Tiantan Hospital, Capital Medical University, Beijing, China. All patients had signed the informed consent before enrollment.

We examined 58 patients from February 2012 to February 2013 with acute ICH (within 6 hours after symptom onset). All patients underwent a non-contrasted computed tomography (CT), CTP, and CTA (CT stroke series) of the head emergently. And also the follow-up non-contrast CT scan was usually obtained on the day after admission as a routine procedure. Patients were excluded from this study if the hemorrhage was secondary to vascular malformation, impaired coagulation, head trauma, hemorrhagic infarction, or those with ICH caused by bleeding into a tumoral lesion.

CT technique

The non-contrast CT was performed immediately before

the CTP to diagnose ICH. All of the initial non-contrasted CT, CTP and CTA, and follow-up non-contrast CT were performed on a 16-section scanner (Sensation, Siemens Medical Solutions, Forchheim, Germany). Non-contrast CT was obtained with 5-mm slice thickness for the posterior fossa and 9-mm slice thickness for the cerebral hemispheres using imaging parameters of 120 kVp, 360 mAs, 1.5-mm section collimation, and 1-second rotation. CTP was obtained with two adjacent 12-mm sections centered at the level of maximum extent of the hematoma. A 40-second cine series was performed beginning 4 seconds after intravenous injection of a compact bolus of 40 ml nonionic iodinated contrast agent (iopamidol, 300 mg iodine/ml; Shanghai Bracco Sine Pharmaceutical Co. Ltd., China) at 8 ml/s by a power injector. CTP imaging parameters were 80 kVp, 209 mAs, 0.5-second rotation, and 40 images per section. Then the patients underwent CTA of the whole brain. Another 90 ml contrast medium (iopamidol, 300 mg iodine/ml) was injected at a rate of 4 ml/s followed by another 60 ml at 3 ml/s. After a delay of 17 seconds, spiral scanning was performed, with the following parameters: beam collimation 0.75×16 mm, slice width 0.75 mm, spiral pitch 1.0, 140 kVp, and 100 mAs. For diagnosis, we used the CTA-SI of 0.75-mm thickness.

Data processing

At the time of acquisition, each patient's CT images were transmitted to picture archiving communication systems (PACS, Neusoft Co. Liaoning, China). In our study, the non-contrast CT images and CTP dynamic raw data, in DICOM 3.0 standard form, were downloaded onto a PC via PACS network. Then hematoma volumes were determined from non-contrast CT images using volume determination software (individual-specific software). And perfusion parameter images, including cerebral blood flow, cerebral blood volume, mean transit time (MTT), and time-to-peak, were calculated using perfusion imaging software (individual-specific software).⁵

Data analysis

For CTP parameter images, the perfusion of hematoma region and perihematoma region was evaluated for presence or absence of the perihematoma penumbra. Three kinds of perihematoma perfusion typing were defined. The imaging criteria were as follows:

Normal group: perfusion abnormal area is only in the hematoma region, and the perfusion of perihematoma region is normal (Fig. 1).

Mild group: perfusion abnormal area is larger than hematoma region, and mismatch of CTP-MTT/non-contrast

CT >20%. But the perfusion abnormalities do not involve the cerebral hemisphere (Fig. 2).

Severe group: perfusion abnormal area includes the whole ipsilateral cerebral hemisphere (Fig. 3).

On CTA-SI, the spot sign was defined as 1 or more 1- to 2-mm foci of enhancement within the hematoma (Fig. 4).⁶ An increase of hematoma size >33% was considered significant enlargement.⁷

Statistical analysis

Statistical analysis was performed using SPSS for windows software version 13.0. Hematoma size between the normal, mild, and severe groups was compared with independent-samples *t* test. A value of $P < 0.05$ was considered significant.

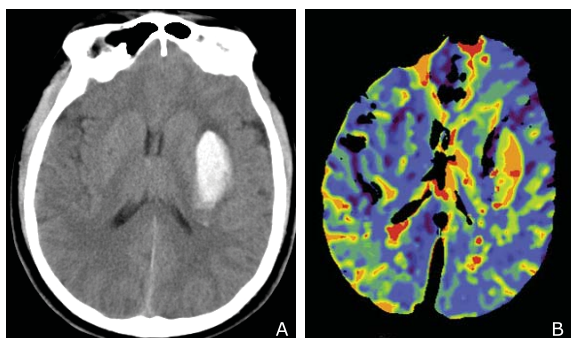


Figure 1. Computed tomography (CT) images of acute intracerebral hemorrhage patient in the normal group.

A. Non-contrasted CT shows hemorrhage in the left basal ganglia with mild surrounding edema.

B. Mean transit time color map shows perfusion abnormal area is only in the hematoma region, and the perfusion of perihematoma region is normal.

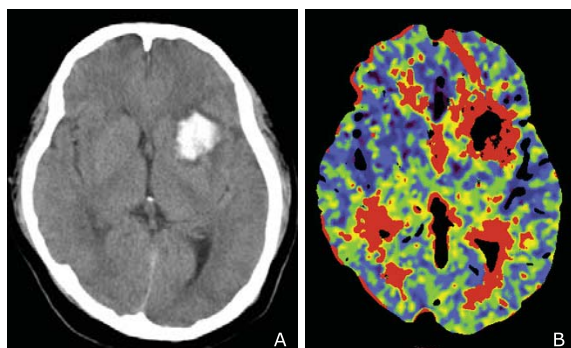


Figure 2. CT images of acute intracerebral hemorrhage patient in the mild group.

A. Non-contrasted CT shows hemorrhage in the left basal ganglia with mild surrounding edema.

B. Mean transit time color map shows perfusion abnormal area is larger than hematoma region, but the perfusion abnormalities do not involve the cerebral hemisphere.

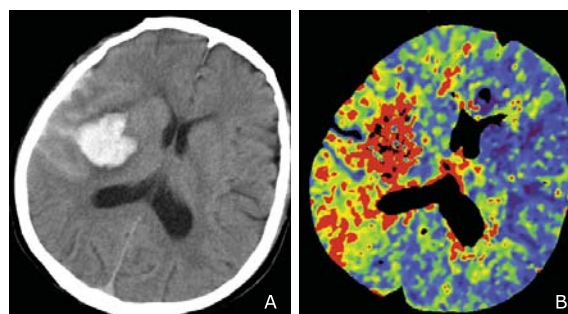


Figure 3. CT images of acute intracerebral hemorrhage patient in the severe group.

A. Non-contrasted CT shows hemorrhage in the right basal ganglia with mild surrounding edema and subarachnoid hemorrhage.

B. Mean transit time color map shows perfusion abnormal area includes the whole ipsilateral cerebral hemisphere.

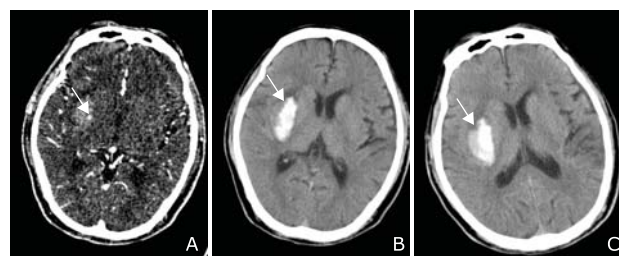


Figure 4. Patient with spot sign and hematoma enlargement.

A. A small focus of enhancement is seen peripherally on CT angiography source image, consistent with the spot sign (arrow).

B. Non-contrasted CT shows hematoma in the right basal ganglia with mild surrounding edema (arrow).

C. Non-contrasted CT image 1 day after presentation reveals hematoma enlargement (arrow).

RESULTS

Of the 58 consecutive patients, 53 patients (34 males, 19 females) were included in our study, and 5 patients were excluded for vascular malformation. Age of the patients ranged from 37 to 76 years, with a mean age of 54.3 ± 11.9 years. The location of hematomas was as follows: basal ganglia in 30 (56.6%) patients, thalamus in 14 (26.4%), lobes in 4 (7.5%), brain stem in 3 (5.7%), and cerebellum in 2 (3.8%).

The 53 patients were classified into 3 groups by perihematoma perfusion typing on CTP parameter images: 21 (39.6%) patients in the normal group, 23 (43.4%) in the mild group, and 9 (17.0%) in the severe group. There were significant differences in the hematoma size between the normal and mild groups (8.91 ± 7.14 and 20.42 ± 17.97 ml, $P < 0.05$). There are significant differences in the hematoma

size between the normal group and severe group (33.98 ± 18.76 ml, $P < 0.05$). There are no significant differences in the hematoma size between the mild group and severe group ($P > 0.05$).

Thirteen (24.5%) patients presented with spot sign. Hematoma expansion occurred in 15 (28.3%) patients on follow-up. The sensitivity of CTA spot sign forecasting hematoma enlargement was 80.0% (12/15), the specificity was 97.4% (37/38). The positive predictive value of CTA spot sign forecasting hematoma enlargement was 92.3% (12/13), the negative predictive value was 92.5% (37/40).

The perihematoma perfusion typing of the patients with or without spot sign is given in Table 1.

Table 1. Perihematoma perfusion typing of the patients with or without spot sign (n)

Item		Perihematoma perfusion typing			
		Normal	Mild	Severe	Total
Spot sign	Positive	3	5	5	13
	Negative	18	18	4	40
	Total	21	23	9	53

DISCUSSION

It had been reported that penumbra of progressive tissue damage develops in regions immediately surrounding a hematoma⁸ and may still exist during the subacute and chronic phases after ICH.⁹ In our study, we found hypoperfusion surrounding a hematoma. But the volume of hypoperfusion is different in patients. So we defined them into three types: the normal group, mild group and severe group. These results suggest that the potential for perihematomal ischemia is different in patients. Some patients may have higher risk and more brain tissue to develop into ischemia penumbra surrounding a hematoma than other patients. The pathological mechanism has not been clarified. But the phenomena may help us to choose appropriate treatment for every patient.

The CTA spot sign is associated with the presence and extent of hematoma progression.¹⁰ Our study confirmed CTA spot sign can highly forecast hematoma enlargement. It has higher sensitivity and specificity. The sign is easily and reliably detected. The presence of this sign may be a useful radiological marker that should be helpful in choosing proper treatment.

The treatment for ICH should transform from experience-based medicine to evidence-based medicine, and then to individualizing therapy. According to the

imaging findings, this preliminary study suggests that we can classify the acute ICH more specifically by CTP and CTA-SI. Furthermore, we hypothesized that there should be different treatment for any ICH patients according to their different appearance on CTP and CTA-SI. For example, a patient was divided into the mild group or severe group on CTP, which meant there was perfusion abnormal area around the hematoma. If treatment was inappropriate, this area may develop into ischemia. If this patient's CTA spot sign was negative, that meant little risk for hematoma enlargement, slightly elevated BP and improved microcirculation treatment may be helpful. On the other hand, if a patient was divided into the normal group on CTP, as well as presence of CTA spot sign, that meant no perihematomal penumbra and high risk for hematoma enlargement, reduced BP and hemostasis therapy were appropriate for this patient.

In conclusion, we found more than 60% patients of acute ICH had perihematomal hypoperfusion (the mild group and severe group), with or without CTA spot sign. In acute ICH patients, the perihematoma perfusion typing and CTA spot sign provide more radiological information that might assist in individualizing therapeutic decisions for patients by possibly forecasting perihematomal ischemia and hematoma enlargement. In further study, we will research the association between perihematomal hypoperfusion and clinical symptoms as well as outcomes.

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