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Comparison of hematoma density heterogeneity and ultraearly hematoma growth in predicting hematoma expansion in patients with spontaneous intracerebral hemorrhage

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ABSTRACT

Background: Hematoma density heterogeneity (HDH) and ultraearly hematoma growth (uHG) are novel imaging predictors for hematoma expansion (HE) based on computed tomography (CT). This study was aimed to compare the accuracy of HDH and uHG in HE prediction within a cohort of spontaneous intracerebral hemorrhage (sICH) patients.

Methods: This study included sICH patients with initial CT within 6 h after onset. uHG was defined as baseline hematoma volume/onset-to-CT time (ml/h) and the cutoff was 4.7 ml/h. HDH was evaluated following a 5-point categorical scale and HDH grade was dichotomized into homogeneous (1–2) and heterogeneous (3–5). The predictive accuracy of HDH and uHG was analyzed by receiver-operator analysis.

Results: A total of 137 patients were included in this study. The mean uHG and median HDH grade were significantly higher in patients with HE. In multivariable analysis, uHG ≥ 4.7 and HDH grade ≥ 3 were associated with HE independently. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of uHG ≥ 4.7 were 76.5%, 57.3%, 37.1%, and 88.1%, respectively. The sensitivity, specificity, PPV and NPV of HDH grade ≥ 3 were 55.9%, 70.9%, 39.8% and 83.0%, respectively.

Conclusions: Both HDH and uHG are promising predictors for HE. HDH has higher specificity while uHG is more sensitive.

1. Introduction

Spontaneous intracerebral hemorrhage (sICH) is the second most common type of stroke, accounting for 10–15% of the all stroke cases every year [1]. Although the incidence of sICH appears to have decreased in recent years, the mortality is still high in sICH patients and only 12%–39% of the survivors live independently after 6 months [2]. Hematoma expansion (HE) is associated with poor prognosis in sICH patients [3,4]. HE can potentially be modifiable and the identification of simple and effective radiological predictors for HE may be has important clinical significance for sICH patients [5]. The spot sign on computed tomography angiography (CTA), which occurs due to active contrast extravasation into the hematoma, has been shown to be a reliable indicator for HE in several previous studies [6–8]. Another predictor based on CTA, the leakage sign, has also been found to be a predictor for HE in sICH patients [9]. Although these HE predictors on CTA seem to have satisfying accuracy for HE prediction, CTA is still unavailable to many patients in the first several hours after symptom onset. Thus, the imaging predictors based on non-contrast computed tomography (NCCT) are still necessary to be investigated. Several HE predictors on NCCT have been reported in recent studies, such as irregular margin [10], fluid levels [10], blend sign [11], black hole sign [12] and hypodensities within hematoma [13]. Particularly, several previous studies reported the hematoma density heterogeneity (HDH) could assist in the prediction of HE [10,14,15]. Previous studies found HDH to be a better predictor of HE compared to irregular margin or fluid levels [13,15]. Moreover, some novel predictors such as blend sign, black hole sign and hypodensities can be considered as special subtypes of HDH as defined in previous studies [11–13]. Recently, Rodriguez-Luna et al.'s study showed the adjustment of baseline ICH volume by onset to baseline CT time, ultraearly hematoma growth (uHG), was a useful predictor

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of HE in sICH patients [16]. However, the predictive accuracy of HDH and uHG has not been compared in the same cohort of sICH patients. Thus, this study was performed to compare the predictive accuracy of HDH and uHG in predicting HE in sICH patients.

2. Methods

2.1. Study design and patients

This study was based on the prospective sICH database in the Department of Neurosurgery, West China Hospital, Sichuan University and was approved by the Biomedical Ethics Committee of West China Hospital. All procedures in this study were in conformity with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All patients or their legal relatives were fully informed and signed informed consent. The inclusion criteria included: (1) adult patients with sICH diagnosed by computed tomography (CT) or magnetic resonance imaging (MRI) scans; (2) initial diagnostic CT performed within 6 h after the onset of sICH; (3) follow-up CT performed within 24 h after initial CT. The exclusion criteria were:(1) intracerebral hemorrhage caused by intracranial aneurysm, arteriovenous malformation, moyamoya disease, infarction or tumor; (2) unavailable initial CT or follow-up CT; (3) patients that received surgical hematoma evacuation before follow-up CT; (4) unclear onset-to-initial CT time. Patients were treated in the special stroke unit and managed following the latest American Heart Association/American Stroke Association (AHA/ASA) and European Stroke Organisation (ESO) guidelines [17,18].

2.2. Clinical data

Patients' baseline information including age, gender, blood pressure at admission, onset-to-initial CT time (OIT) and medical history was collected. Medical history included hypertension, diabetes mellitus, previous stroke, Warfarin use and smoking and alcohol abuse. Results of coagulation tests at admission, including platelet count, prothrombin time (PT), international normalized ratio (INR) and activated partial thromboplastin time (APTT), were also collected.

2.3. Imaging acquisition and detection of imaging markers

The initial CT scan (120 kV, 340 mA, contiguous 5-mm axial slices) was performed on a dual-source 64-slice CT scanner (SOMATOM Definition Flash; Siemens Healthcare Sector, Forchheim, Germany). A follow-up CT was performed within 24 h after the initial CT. Two neuroradiologists (M. L. and X. W.), blinded to the patients' clinical conditions, independently reviewed all CT scans. The initial CT and the follow-up CT were evaluated separately. If a disagreement about imaging markers occurred, it would be solved by consensus. HDH was evaluated based on a 5-point categorical scale as follow: (1) the scale ranged from Category 1 (most homogeneous density) to Category 5 (most heterogeneous density).); (2) hematoma with more heterogeneous density than represented on the scale would be rated as Category 5; (3) intraventricular hemorrhage (IVH) was not included in the scale rating [15]. The grade of HDH was dichotomized into homogeneous (1–2) and heterogeneous (3–5). Fig. 1 showed the baseline and follow-up CT scans of a typical case with heterogeneous density marked as Category 5. To provide more information, other predictors of HE on NCCT, including blend sign, black hole sign, margin irregularity, fluid levels and hypodensities within hematoma were also evaluated according to previously studies [10–13,15].

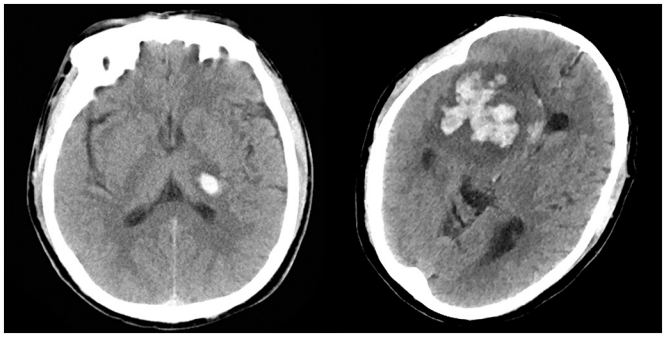

Fig. 1. Examples of homogeneous density marked as Category 1 (left) and heterogeneous density marked as Category 5 (right).

2.4. Measurement of hematoma volume

Hematoma volume was calculated from CT scans using the ABC/2 method, in which A was the largest diameter on the largest hemorrhage slice, B was the maximal diameter perpendicular to A, and C was the vertical hematoma depth [19]. uHG was calculated by dividing the baseline hematoma volume onset-to-initial CT time [20]. The cutoff of uHG for predicting HE was 4.7 ml/h as reported previously [16]. HE was defined as a > 33% relative increase or > 12.5 ml absolute increase in hematoma volume on follow-up CT scan [21].

2.5. Statistical analysis

All data in this study was analyzed using SPSS 22.0 and Excel 2016. Baseline information was compared between patients with HE and those without HE, including age, gender, medical history, blood pressure at admission, hematoma characteristics at admission and coagulation tests at admission. If P value was <0.5, statistical significance was assumed. Continuous values were expressed as mean and standard deviation (SD) and analyzed by the *t*-test. Discontinuous variable data were expressed as median and interquartile range (IQR) and analyzed by the Wilcoxon rank sum test. The categorical values were analyzed by chi-square analysis. Multivariable logistic regression was performed to adjust the odds ratio (OR) and 95% confidence interval (CI) of uHG and HDH on HE. Variables which were reported to be associated with HE previously or had $P < 0.10$ in univariable analysis were included in multivariable analysis. The volume of hematoma and OIT were excluded for they were components of uHG. The values of uHG and HDH for predicting HE were analyzed by receiver-operator analysis. The area under the receiver-operating characteristic (ROC) curves of different predictors was compared with the Z test. The interobserver reliability for the identification of HDH grade was determined by κ values and $\kappa > 0.8$ was considered as the perfect interobserver reliability [22].

3. Results

From February 2015 to May 2016, a total of 137 patients met the inclusion criteria and were enrolled in this study. The median time interval from sICH onset to initial CT was 4 h (3, 5 h). Enrolled subject age ranged between 36 and 83 years (mean 59.5 ± 12.0 years). The mean baseline volume of hematoma was 23.9 ± 20.9 ml. Positions of hematoma included lobar (21, 15.3%), basal ganglia (78, 56.9%), thalamus (16, 11.7%), cerebellum (6, 4.4%) and brain stem (16, 11.7%). HE was observed in 34 out of 137 patients. The mean volume of HE was 22.5 ± 22.0 ml. The baseline characteristics of HE group and non-HE group were shown in Table 1. In our study, the mean uHG was 6.6 ± 6.2 ml/h and 70 patients had uHG > 4.7 ml/h. The median grade of HDH was 2 (1,3) and 40 patients had a grade of HDH ≥ 3. In this study, the mean uHG and median grade of HDH were significantly higher in patients with HE compared with those without HE. Interobserver reliability for the identification of HDH grade was excellent between the two neuroradiologists ($\kappa = 0.938$). The multivariate analysis displayed that uHG ≥ 4.7 and grade of HDH ≥ 3 were independently associated with HE (Table 2).