MRI Profile of the Perihematomal Region in Acute Intracerebral Hemorrhage

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Background and Purpose—The pathophysiology of the presumed perihematomal edema immediately surrounding an acute intracerebral hemorrhage is poorly understood, and its composition may influence clinical outcome.

Method—Twenty-three patients from the Diagnostic Accuracy of MRI in Spontaneous intracerebral Hemorrhage (DASH) study were prospectively enrolled and studied with MRI. Perfusion-weighted imaging, diffusion-weighted imaging, and fluid-attenuated inversion recovery sequences were coregistered. TMax (the time when the residue function reaches its maximum) and apparent diffusion coefficient values in the presumed perihematomal edema regions of interest were compared with contralateral mirror and remote ipsilateral hemispheric regions of interest.

Results—Compared with mirror and ipsilateral hemispheric regions of interest, TMax (the time when the residue function reaches its maximum) and apparent diffusion coefficient were consistently increased in the presumed perihematomal edema. Two thirds of the patients also exhibited patchy regions of restricted diffusion in the presumed perihematomal edema.

Conclusion—The MRI profile of the presumed perihematomal edema in acute intracerebral hemorrhage exhibits delayed perfusion and increased diffusivity mixed with areas of reduced diffusion. (Stroke. 2010;41:2681-2683.)

Key Words: intracerebral hemorrhage ■ MRI

Perihematomal edema occurs within the first few days after intracerebral hemorrhage (ICH) onset. Experimental studies suggest that the mechanism of perihematomal edema formation is multifactorial and may be of cellular (cytotoxic) or vasogenic origin. Multimodal MRI can help characterize presumed perihematomal edema (PPE). Vasogenic edema increases the apparent diffusion coefficient (ADC), and cytotoxic edema decreases ADC on diffusion-weighted imaging. Perfusion-weighted imaging (PWI) can identify critically hypoperfused regions. Previous MRI studies consistently demonstrated hypoperfusion in the PPE, but studies of diffusion-weighted imaging have reported conflicting results. One study found decreased ADC in the PPE, whereas 3 others concluded that ADC was globally increased.

We investigated the MRI profile of PPE of 20 consecutive patients in the Diagnostic Accuracy of MRI in Spontaneous intracerebral Hemorrhage (DASH) study.

Methods

Patients
The DASH study is a prospective National Institutes of Health (NIH)–funded study that aims to assess the feasibility and diagnostic yield of routine brain MRI in spontaneous (nontraumatic) ICH. Inclusion criteria for this substudy of 23 consecutive patients were: supratentorial ICH, no brain surgery before MRI, and MRI within 3 days after symptom onset, including diffusion-weighted imaging, PWI using multiecho multishot parallel imaging,10 and fluid-attenuated inversion recovery (FLAIR). Three patients with technically inadequate PWI were excluded.

MRI Protocol
The brain MRI protocol has been described previously.10

Coregistration and Region of Interest Generation
MRIs were analyzed using Medical Image Processing Analysis and Visualization software. The coregistration process and PPE definition are illustrated in Figure 1. Relative ADC was defined as the mean ADC value of the ipsilateral region of interest (ROI) divided by the mean ADC value of its mirror ROI. Restricted diffusion lesions were qualitatively identified by a hyperintense signal on B1000 and a corresponding hypointense signal on ADC map within the PPE.

Statistical Analysis
Wilcoxon signed-rank or Friedman test and Mann–Whitney U tests were used to compare related and nonrelated volumes, time to maximum plasma concentration (TMax), and ADC values. The Spearman Rank test was used to estimate the correlation. The Fisher...
exact and McNemar tests were used to compare independent and related proportions. All tests were 2-tailed, and statistical significance was defined as $\alpha=0.05$. Descriptive data are presented as median (interquartile range) values except when specified otherwise.

## Results

### Baseline Characteristics

Baseline characteristics of the 20 included patients are presented in the Table.

### Perfusion Imaging

In regions of PPE, the TMax delay of 5.7 seconds (4.7 to 7.2) was higher compared with the corresponding contralateral mirror ROI (3.5 seconds; 2.9 to 4.5; $P<0.001$) and the ipsilateral hemisphere ROI (3.7 seconds; 3.2 to 4.5; $P<0.001$; Figure 2A). PPE TMax delay was higher in patients scanned within 24 hours after symptom onset ($n=10$; $P=0.017$). Among the 7 patients with a mean TMax delay $>6$ seconds, ICH volumes on FLAIR were larger (49 mL; 19 to 60) compared with the remaining patients (14 mL; 8 to 18; $P=0.046$), however, edema volumes were not different.

### Diffusion Imaging

The mean ADC measured in the PPE ($1026 [972 to 1099] \times 10^{-6} \text{mm}^2/\text{s}$) was higher than the mirror ROI ($895 [801 to 1033] \times 10^{-6} \text{mm}^2/\text{s}$; $P=0.004$), and the ipsilateral hemisphere ROI ($878 [802 to 962] \times 10^{-6} \text{mm}^2/\text{s}$; $P<0.001$; Figure 2B). In the PPE, relative ADC (1.16 [1.04 to 1.28]) was higher compared with the relative ADC measured in the

### Table. Baseline Characteristics

| Age, mean (SD), y | 61 (17) |
| NIH Stroke Scale | 12 (5–20) |
| Glasgow Coma Scale | 14 (7–15) |
| Topography deep/lobar | 11/9 |
| MRI FLAIR volume, mL | 23 (12–58) |
| MRI T2* volume, mL | 27 (21–81) |
| Time from symptom onset to MRI, hours | 26 (12–64) |
| Edema volume, mL | 22 (10–33) |
| Edema ROI volume, mL | 14 (8–26) |
| Hemisphere ROI volume, mL | 34 (30–42) |
| ICH cause | Primary: hypertension (11), possible cerebral amyloid angiopathy (3), unknown (1) Secondary: vascular malformation (3), cerebral venous thrombosis (1), hemorrhagic transformation of an infarction (1) |

Figure 1. ROI generation. 1, FLAIR was coregistered to T2* PWI (first echo time). PPE was outlined on FLAIR and then transposed to T2* PWI. 2, All the hyperintense signal caused by blood on T2* was removed from the PPE ROI to avoid contamination of the PWI maps. Ipsilateral hemisphere ROI was drawn in the spared hemisphere. 3, Both ROIs were flipped on the opposite hemisphere. 4, ROIs were transposed on PWI maps to measure mean TMax value (same process was performed with ADC map).

Figure 2. Mean TMax value (A), mean absolute ADC (B), and relative ADC (C) in the PPE, its corresponding opposite ROI, in the ipsilateral hemisphere and its corresponding ROI in the opposite hemisphere.
MRI Profile According to ICH Cause

Patients with both primary and secondary causes of ICH exhibited a delayed Tmax and increased ADC in the PPE.

Among the 14 patients with restricted diffusion lesions in the PPE, ICH causes were hypertension (10), cerebral amyloid angiopathy (1), vascular malformation (2), and hemorrhagic transformation of brain infarction (1).

Discussion

Our results demonstrate a consistent MRI profile in the region of PPE surrounding acute ICH: significant perfusion delay and facilitated diffusion mixed with patchy areas of restricted diffusion.

Perihematoma hypoperfusion was inversely related to time from symptom onset and associated with large ICH volumes as shown previously.5–8 One third of our patients exhibited a Tmax of more than a 6-second delay, which has been associated with critical hypoperfusion in brain infarction.4

ADC maps suggest that PPE consists of areas with cytotoxic and vasogenic edema. Interestingly, the presence of cytotoxic edema was found in the majority of patients with a primary ICH cause. It was associated with hematoma size but not with the severity of hypoperfusion. These findings suggest that cytotoxic edema in the PPE might be related to ICH mass effect or the accumulation of cytotoxic factors such as thrombin or iron rather than hypoperfusion.2

Our study has several limitations. First, MRI was performed 1 to 3 days after ICH onset (ie, after the majority of ICH expansion has occurred). Imaging performed at an earlier time point might yield different results. Second, we chose Tmax as the perfusion parameter to assess hypoperfusion. Another option would have been to use mean transit time. Tmax maps provide better signal-to-noise ratio compared with the mean transit time maps, and recent data suggest that Tmax may better represent critical tissue hypoperfusion than mean transit time.4 Finally, our results derived from a small sample size need confirmation in a larger study and do not allow for analyzing correlations between MRI profile and functional outcome.

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Disclosures

None.

References

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