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Diffusion Tensor Imaging Predicts Motor Functional Outcome after Acute Hypertensive Intracerebral Hemorrhage

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Abstract

Early evaluation of the corticospinal tract (CST) is critical for patients with acute hypertensive intracerebral hemorrhage (ICH) to predict long-term motor functional outcome. Therefore, we investigated motor functional outcome of an ICH using diffusion tensor imaging (DTI) in patients with hypertensive ICH. Thirty six patients with hemiparesis due to hypertensive ICH underwent DTI within 3 days after onset. Fractional anisotropy (FA) was measured within the CST at levels of the posterior limbs of the internal capsules, and motor impairment was assessed on admission and 8 weeks after ICH by manual muscle test. The correlation between FA ratio and improvement of motor function was analyzed by Pearson's correlation analysis. The FA ratio from the initial DTI showed a correlation with motor function improvement. The amount of hematoma correlated with motor function on admission, but did not show correlation with the degree of motor recovery. Therefore, FA ratio analysis calculated from FA values of DTI could be a prognostic factor of motor function improvement in patients with hypertensive ICH.

Keywords: Hypertensive intracerebral hemorrhage; Diffusion tensor imaging; Corticospinal tract; Motor impairment

Introduction

Hypertensive intracerebral hemorrhage (ICH) may be accompanied by various degrees of motor function deficits. The most common locations of hypertensive ICH are basal ganglia (BG), thalamus, and cerebellum. The main type of motor impairment resulting from hypertensive ICH is damage to the corticospinal tract (CST). Particularly, posterior limb of the internal capsule is frequently affected by hypertensive ICH in the BG and thalamus. Previous studies have attempted to predict motor function outcome by analyzing CST state during the early stages of ICH [1-5] and diffusion tensor imaging (DTI) has received increasing attention.

DTI is a promising method for characterizing microstructural changes or difference of brain tissues and the diffusion tensor may be used to characterize the magnitude, anisotrophy and orientation of the diffusion tensor [6]. Each of different neural fiber has different directions by which diffusion directions are affected, and it is visualized using DTI. Those different neuronal fiber directions could be analyzed using DTI and clinically it could be applied to some white mater diseases. Estimates of white matter connectivity patterns in the brain from white matter tractography may be obtained using the diffusion anisotropy and the principal diffusion directions [6-9]. Prediction of motor function outcome after hypertensive ICH is critical for patients and doctors. Computed tomography (CT) scan and magnetic resonance imaging (MRI) can evaluate the amount of hematoma and location of hematoma, but these techniques are difficult to determine the motor functional outcomes.

Thus, we performed DTI within 3 days following hypertensive ICH and attempted to elucidate the correlation between the extents of the damage of CST passed through posterior limb of the internal capsule and motor functional outcome of patients with hypertensive ICH at 8 weeks after onset.

Materials and Methods

Patients

From January 2014 to December 2014, DTI was performed on 36 patients with hypertensive ICH within 3 days after ICH. The inclusion criteria were as follows: (1) hypertensive ICH in BG and/or thalamus as diagnosed by CT scan; (2) motor deficit present at the time of admission; (3) no previous history of stroke, traumatic brain injury, or other brain disease. This study was approved by our institutional review board and informed consent was obtained from all patients.

Clinical assessment and magnetic resonance imaging

Motor impairment was evaluated according to the severity of motor paresis, which was estimated at the time of admission and 8 weeks after ICH. Motor functions of each patient were examined by manual motor test graded as 0 to 5 points at both upper and lower extremities.

Hypertensive ICH was diagnosed based on initial brain CT scan with thickness of 4.5 mm. The amount of hematoma was calculated by recording the largest diameter seen on CT, the diameter orthogonal to it, and the number of 4.5 mm slices on which the hematoma could be seen. The total volume was estimated using the formula for an ellipsoid, ABC/2, where A, B, and C represent the respective diameters of the 3 dimensions [10]. DTI was performed using a 1.5-T Magnetom Sonata Maestro Class scanner (Siemens, Erlangen, Germany). The DTI data was acquired using a single-shot echo-planar imaging sequence (repetition time, 12,100 ms; echo time, 100 ms; field of view, 256 mm; number of excitation, 1; matrix 128 × 128; and 2 mm thickness. The

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DTI was performed within 3 days following ICH onset. Figure 1 reveals initial brain CT scan, tractography, and FA map of patient #36, who showed no motor recovery at last follow-up.

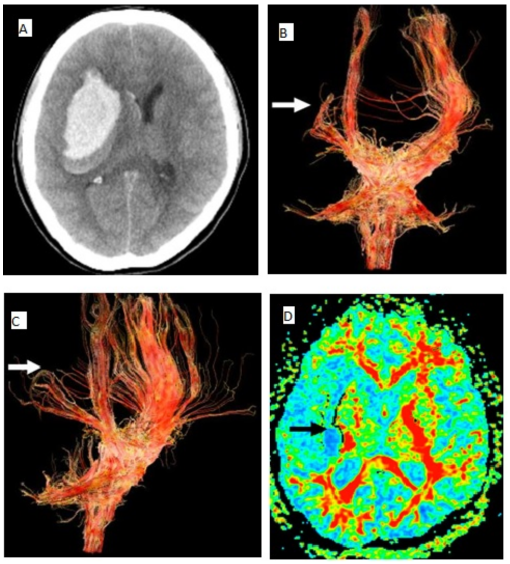

Figure 1: Images obtained from a 62 year-old woman (Patient #36) who showed no poor motor recovery. Brain computed tomography (A) shows hypertensive intracerebral hemorrhage at the right basal ganglia. Coronal (B) and sagittal (C) views of tractography reveals disrupted corticospinal tract on the right side by a hematoma. The fractional anisotrophy map (D) demonstrates a destruction of fractional anisotrophy in the posterior limb of internal capsule.

Data processing

The fractional anisotrophy (FA) for analyzing the extent of the affected by measuring the region of interest (ROI) in the FA map [2,11]. In addition, the ratio of the FA between the affected and affected sides was calculated. FA ratio was defined as the proportion of FA value of injured posterior limb of the internal capsule (b) to FA value of non-injured (a), and calculated as follows: FA ratio (%)=b/a × 100.

Statistical analysis

All statistical analyses were performed using SPSS software version 17.0 (SPSS Inc, Chicago, IL). Each result of manual motor test values were compared with FA ratio and relations were analyzed by Pearson's correlation analysis. Analysis of motor function with the amount of hematoma was also preformed with Pearson's correlation analysis. And other factors, such as hypertension and diabetes were also analyzed the relationship with motor function by linear-by-linear association. A multivariate liner regression model was applied to study the associations with the regard on independence. A p value less than 0.05 was considered statistically significant.

Results

Male female ratio was 1.4:1 (male 21 and female 15) and mean age was 67.5 years old. Twenty-six patients underwent surgery (23 stereotactic surgeries, 3 craniotomy surgeries) and 10 patients were treated conservatively. Locations of hematoma were BG in 24 patients, thalamus in 11 patients, and both of these in 1 patient. The patients' data included in this study were summarized in Table 1. All patients showed that injured area FA value was lower than normal area FA value. Table 2 shows that the relation between FA ratios and manual motor test values (initial and follow up). In the case of motor power of upper limb, there was significant correlation (p=0.010) on admission day and higher significant correlation (p=0.001) 8 weeks following ICH. On the other hand, the correlation between motor function of lower extremities on admission and FA ratio was not statistically significant (p=0.071), but the correlation between motor function of lower extremities 8 weeks after ICH onset and FA ratio was statistically significant (p=0.006).

No.	Sex	Age	Volume (cc)	operation	HTN	DM	UM/LM* Admission	UM/LM Follow up	FA value**: unaffected	FA value: affected	FA ratio
1	M	77	44	O	N	N	0/2	2/3	0.544	0.535	98.3%
2	F	65	19	O	N	N	3/2	3/2	0.462	0.374	81.0%
3	F	72	5	X	N	N	5/5	5/5	0.347	0.342	98.6%
4	M	69	168	O	N	Y	2/1	4/3	0.496	0.487	98.2%
5	M	69	27	O	N	N	4/4	5/5	0.466	0.442	94.8%
6	M	62	3	X	Y	N	4/4	5/5	0.534	0.364	68.2%
7	M	62	36	O	Y	N	3/4	3/4	0.516	0.501	97.1%
8	M	77	9	X	N	N	4/2	5/5	0.625	0.598	95.7%
9	M	61	43	O	N	N	1/1	0/1	0.428	0.217	50.7%
10	F	68	28	O	N	N	2/4	5/5	0.321	0.317	98.8%
11	F	68	26	O	N	N	2/0	2/4	0.382	0.374	97.9%

12	M	60	36	O	N	Y	3/3	2/2	0.586	0.449	76.6%
13	M	65	65	O	Y	N	2/2	2/2	0.552	0.287	52.0%
14	M	64	9	O	N	N	4/4	4/5	0.520	0.387	74.4%
15	F	70	10	O	N	N	1/2	1/4	0.460	0.346	75.2%
16	F	82	3	X	Y	N	4/4	5/5	0.578	0.461	79.8%
17	F	73	2	X	Y	N	4/4	4/5	0.293	0.272	92.8%
18	M	68	8	O	N	N	2/3	2/3	0.447	0.313	70.0%
19	M	69	25	O	Y	N	1/2	1/2	0.495	0.350	70.7%
20	M	62	25	O	Y	N	1/2	1/2	0.521	0.489	93.9%
21	M	83	3	X	N	N	3/3	5/5	0.609	0.586	96.2%
22	M	64	18	O	N	N	2/4	3/5	0.501	0.427	85.2%
23	F	69	6	O	Y	N	1/2	1/3	0.481	0.371	77.1%
24	M	67	20	O	Y	N	1/2	2/3	0.542	0.405	74.7%
25	M	67	18	O	N	N	1/2	1/3	0.413	0.210	50.8%
26	M	62	66	O	Y	N	3/1	4/1	0.312	0.303	97.1%
27	F	61	10	O	N	N	2/3	4/4	0.411	0.394	95.9%
28	F	68	8	X	N	N	2/3	2/3	0.481	0.401	83.4%
29	M	68	110	O	N	N	1/2	5/5	0.495	0.295	59.6%
30	M	64	7	X	Y	Y	4/4	4/4	0.461	0.452	98.0%
31	F	72	8	X	Y	Y	3/3	3/3	0.394	0.332	84.3%
32	F	68	10	O	N	N	3/3	5/5	0.551	0.542	98.4%
33	M	62	41	O	N	N	2/2	4/4	0.341	0.304	89.1%
34	F	66	2	X	Y	N	4/4	5/5	0.410	0.395	96.3%
35	F	65	31	O	Y	N	1/1	1/1	0.391	0.243	62.1%
36	F	62	49	O	Y	N	1/1	1/1	0.431	0.274	63.6%

*UM: Upper Motor; LM: Lower Motor; **FA: Fraction Anisotropy
Y: Yes; N:No; HTN: Hypertension; DM: Diabetes Mellitus

Table 1: The patients' data included in this study.

Therefore we could determine that FA ratio was significantly correlated with motor function improvement. The correlation between motor function and volume of hematoma was statistically significant on admission (p=0.044 and p=0.002), however, there was no statistically significant correlation 8 weeks after ICH (p=0.891 and p=0.076). The correlation of other factors (hypertension and diabetes) with motor function was summarized in Table 3.

In these results, there were no statistically significant correlations between other factors and motor function. When the effects of FA ratio from the DTI on motor recovery were examined with regard on independence in a multivariate linear regression model, only FA ratio remained as a significant independent factor (p=0.005; F=12.4; r^2=0.41; Table 4).

	UM adm*	UM F/U**	LM adm	LM F/U
FA ratio	0.010	0.001	0.071	0.006
Volume	0.044	0.891	0.002	0.076

*UM: Upper Motor; LM: Lower Motor; **FA: Fraction Anisotropy; F/U: Follow-Up

Table 2: Correlation between motor function and FA ratio and volume of hemorrhage.

Discussion

DTI is a technique to display different direction of diffusion in each different neural tissue in diffusion weighted image (DWI). It has been reported that DTI is more sensitive test than DWI in brain white-mater infarction [12]. Moreover, in contrast to conventional MR studies in some cases of diffuse axonal injury without any clinical brain lesion, white-mater damage could be detected by DTI [13].

	UM adm	UM F/U	LM adm	LM F/U
HTN	0.804	0.169	0.593	0.118
DM	0.845	1.000	0.679	0.463

Adm: Admission,*UM: Upper Motor; LM: Lower Motor; **FA: Fraction Anisotropy; F/U: Follow-Up; HTN: Hypertension; DM: Diabetes Mellitus

Table 3: Correlation between motor function and hypertension and diabetes.

In patients with cerebral infarction, several studies have shown that the DTI could identify the structural changes including motor fibers in CST [14]. Additionally, the DTI could provide useful information in tumor patients [15-17]. Therefore, the DTI appears to be a method to investigate the neuronal and axonal fiber damages in the posterior limb of the internal capsule, and FA ratio has been used as a prognostic factor of motor function [18]. Furthermore, it has been suggested that the motor function recovery following ICH could be estimated by investigating the state of the CST using DTI [1-5,10].

Variable	β*	p
FA ratio†	0.648	0.005
Hypertension	-0.354	0.270
Diabetes mellitus	-0.311	0.337
Hemorrhage volume	0.307	0.189
Age	0.173	0.540
Sex	0.237	0.256
Motor grade on admission	0.253	0.201
Surgery	-0.132	0.539
Admission time	0.017	0.928

β* indicates the standardized partial regression coefficient, †Only variables with $p<0.05$ entered into the model; $F=12.4$, $p=0.005$; $r^2=0.41$; FA : Fraction Anisotropy

Table 4: Multivariate linear regression analysis to predict motor recovery at 8 weeks after intracerebral hemorrhage.

In the present study, we determined the correlation between the motor impairment due to ICH and the FA ratio from DTI. The patients with high FA ratio showed good motor recovery even though the severity of initial motor impairment was severe. In contrast, the patients with low FA ratio showed poor recovery even if the initial severity of motor impairment was not severe. In other words, the degree of motor improvement was correlated with the FA ratio, but was not correlated with the initial degree of motor impairment. When the relationship between the amount of hematoma and the degree of motor improvement was examined, we could not find relationship between volume of hematoma and motor function improvement. In general, if there is a large hematoma, there is more possibility of damage to CST including the posterior limb of the internal capsule, thereby increasing in motor impairment. However, even large hematoma could not always give rise to motor impairment if the hematoma does not destruct the CST and only compress the CST, particularly the posterior limb of internal capsule.

Neurological recovery following ICH occurs mainly during the first 2 weeks and over 90% of neurological recovery from stroke takes place in the first 3 months [19,20]. However, in our study, we compared the degree of motor recovery using manual motor test at 8 weeks following ICH. Additionally there are several limitations in this study: (1) we did not consider factors like shape of hematoma, direction, location and circulation which could influence prognosis. (2) There was the possibility of bias in measuring FA because the boundary of measurements was not always the same in all cases. (3) We did not perform follow-up DTI at 8 weeks after ICH to elucidate the longitudinal changes of the injured CST.

Based on our results, FA ratio can reflect injury of posterior limb of the internal capsule of CST, thereby that motor improvement could be estimated by measuring FA ratio from DTI in patients with hypertensive ICH.

Conclusion

In patients with hypertensive ICH, FA ratio that is calculated from FA values of DTI could be a prognostic factor of motor function improvement. The amount of hematoma may be related to motor function on admission, but it is not related to the degree of motor recovery.

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