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Evaluation of Initial Diffusion-weighted Image Findings in Acute Stroke Patients using a Semiquantitative Score

Naomi MORITA^{1*}, Masafumi HARADA², Masaaki UNO³, Shunji MATSUBARA³,
Shinji NAGAIRO³, and Hiromu NISHITANI¹

*Departments of ¹Radiology and ²Radiologic Technology, School of Medicine, University of Tokushima
3–18–15, Kuramoto-cho, Tokushima, Tokushima 770–8503, Japan*

³Department of Neurosurgery, Institute of Health Biosciences, University of Tokushima Graduate School

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Purpose: We evaluated the usefulness of rating diffusion-weighted images (DWI) using a semiquantitative score modified from the Alberta Stroke Programme Early CT Score (ASPECTS) to predict deterioration of neurological symptoms in patients with hyperacute ischemic stroke who had undergone thrombolytic therapy with recombinant tissue plasminogen activator (rt-PA).

Materials and Methods: We examined 22 patients with acute stroke (14 men, 8 women, mean age 72.5 years) treated with intravenous rt-PA. All were assessed using the National Institutes of Health Stroke Scale (NIHSS) and underwent emergent magnetic resonance (MR) imaging within 3 hours and 24 hours of stroke onset. Patients were divided into a deteriorated group (16 patients), in which NIHSS scores were increased after thrombolysis, and a non-deteriorated group (6 patients). We compared the DWI score, ASPECTS, and volume of hyperintense ischemic lesion on DWI (DWI volume) of the 2 groups and examined correlations between these scores and initial NIHSS score or DWI volume.

Results: The DWI score and ASPECTS tended to be lower in the deteriorated group than the non-deteriorated group. In addition, with a cutoff value ≤ 7 , the DWI score could discriminate the deteriorated group from the non-deteriorated group with a sensitivity of 50% and specificity of 87.5%, whereas for ASPECTS, sensitivity was 50% and specificity, 81.2%. The DWI score, ASPECTS, and DWI volume had no correlation with NIHSS score but weak negative correlations with the DWI volume ($P < 0.01$; Spearman's test). Comparing initial NIHSS score with each DWI score and DWI volume, the non-deteriorated group tended to have higher DWI scores and smaller DWI volumes than the deteriorated group, but there was no statistical difference between initial NIHSS and DWI scores. Though the DWI score was not statistically different, the threshold would be set to 6 points or above. Comparing initial DWI score with volume, patients with low DWI scores tended to show large variation in DWI volume and patients with small DWI volume showed large variation in DWI scores. There was no relation between hemorrhagic change and symptoms in either group.

Conclusions: The semiquantitative DWI score easily evaluated extent of acute ischemic lesion on DWI and might be used to predict patient outcome after thrombolytic therapy more accurately than ASPECTS or DWI volume.

Keywords: *acute ischemic stroke, Alberta Stroke Programme Early CT Score, DWI*

Introduction

Thrombolysis with intravenous recombinant tissue plasminogen activator (rt-PA) within 3 hours of

onset of acute ischemic stroke improves patient outcome.^{1,2} Treatment response is highly time dependent; favorable outcome declines rapidly as time from stroke onset increases.² Early ischemic changes on noncontrast computed tomography (CT) have been appreciated and thought to be helpful for predicting the benefit from thrombolysis.^{3–5}

*Corresponding author, Phone: +81-88-633-7173, Fax: +81-88-633-7174, E-mail: nmorita@clin.med.tokushima-u.ac.jp

The extent of ischemic change has been assessed by establishing whether hypoattenuation is present in less or more than one-third of the middle cerebral artery (MCA) territory⁶ or by using the Alberta Stroke Programme Early CT Score (ASPECTS). ASPECTS is a semiquantitative grading that subdivides the MCA territory into 10 regions.⁷ Extensive ischemic change that affect more than one-third of the MCA territory or an ASPECTS ≤ 7 is associated with poor outcome and might reflect an increased risk for thrombolysis-related symptomatic hemorrhage.⁶⁻⁸

ASPECTS was also applied to assess early ischemic lesion on diffusion-weighted images (DWI), but results differed from those by ASPECTS on computed tomography (CT). Recently, the Acute Stroke Imaging Standardization Group in Japan (ASIST-Japan) proposed a semiquantitative score modified from the ASPECTS for evaluating early ischemic lesions on DWI (DWI score), but its performance for predicting patient outcome has not been fully validated. Therefore, we compared the use of DWI score with ASPECTS and volume of the ischemic lesion on DWI in predicting patient outcome after acute ischemic stroke and intravenous administration of rt-PA.

Materials and Methods

From October 1st 2006 to August 31st 2007, we analyzed 22 consecutive patients (14 men, 8 women, mean age 72.5 years. [45 to 88 years]) with acute ischemic stroke in the MCA territories who were treated with intravenous rt-PA.

All patients were assessed using the National Institutes of Health Stroke Scale (NIHSS) and underwent emergent MR imaging within 3 hours of stroke onset. MR imaging was performed on a 3-tesla (3T) clinical machine (Signa Echospeed, General Electronic Medical Systems, Milwaukee WI, USA) equipped with a standard quadrature head imaging coil. Our protocol for emergent MR imaging for acute stroke included DWI, MR angiography (MRA), and T_2^* -WI. Imaging parameters of each sequence were: DWI (repetition time/echo time [TR/TE] 10000/71.8 ms; field of vision [FOV] 28; slice thickness/gap 5/1.5 mm; matrix 128 $\times$ 128; number of excitations [NEX] 1; b factor 1000 s/mm²); MRA (TR/TE 30/3.9 ms, FOV 24, slice thickness/gap 1.2/4 mm, flip angle [FA] 15°, matrix 384 $\times$ 150); and T_2^* -WI (TR/TE 380/29 ms, FOV 24, slice thickness/gap 5/1.5 mm, FA 20°, matrix 512 $\times$ 192). All patients fulfilled the imaging criteria of our institution, including absence of intracranial hemorrhage on initial T_2^* -WI

and hyperintensity less than 1/3 of the MCA territory on initial DWI. Sites of occlusion on MRA were: internal carotid artery (ICA), 6; MCA, 13 (8 M1 occlusion, one M2 occlusion, 4 branch atherosclerotic disease); and unknown, 3 (intact MRA). The cause of ischemia was atherosclerotic in 11, cardioembolic in 10, and unknown in one.

The patients received intravenous administration of 0.6 mg/kg of the rt-PA, alteplase (10% of total dose as bolus injection during first minute and remainder as infusion over 1 hour). The mean time to start rt-PA from symptom onset was 141 min (80 to 179 min). Specific guidelines for monitoring and treating raised blood pressure for the first 24 hours after treatment were provided to all patients. Follow-up NIHSS and MR imaging examinations were performed within 24 hours after starting rt-PA treatment. Existence of intracerebral hemorrhage was evaluated by T_2^* -WI; symptomatic hemorrhage was that associated with increase in NIHSS more than 4 points.

We divided patients into 2 groups by change between initial and follow-up NIHSS; NIHSS increased in the deteriorated group and decreased or was unchanged in the non-deteriorated group.

Two readers with experience using ASPECTS methodology and who completed a detailed tutorial evaluated DWI findings using the DWI score and ASPECTS. They were blinded to clinical information, including side of symptoms, and evaluated scores by consensus. They evaluated the DWI score and ASPECTS using 2 standardized levels, involving the basal ganglionic axial levels and supraganglionic slices. The DWI score included 11 regions: 3 subcortical structures (lentiform, caudate nucleus, and posterior rim of internal capsule), 7 cortical structures (insula, M1 through M6), and one white matter structure (corona radiata); ASPECTS included 10 regions besides the corona radiata (Fig. 1).

In addition, we manually traced the area of hyperintensity on DWI to measure the DWI volume in each slice.

We examined the differences in DWI score, ASPECTS, DWI volume, NIHSS, and other demographic factors between the deteriorated and non-deteriorated groups and compared data between the 2 groups using Student's *t*-test or Wilcoxon nonparametric test. We also used a cutoff value of ≤ 7 to evaluate sensitivities and specificities of DWI score and ASPECTS for differentiating the deteriorated from non-deteriorated group because previous studies associated ASPECTS ≤ 7 with poor outcome. Further, we used Spearman's test to analyze correlations between the DWI score or ASPECTS

Fig. 1. Semiquantitative diffusion-weighted image (DWI) score from modified Alberta Stroke Programme Early Computed Tomography Score (ASPECTS; DWI score). The DWI score divided the middle cerebral artery (MCA) territory into 11 regions, which included white matter. The Acute Stroke Imaging Standardization Group in Japan ASIST-Japan proposed this scoring system for evaluating acute ischemia. (<http://assist.umin.jp/>)

and the DWI volume or NIHSS.

Results

Of 22 patients, six were classified as deteriorated and 16 as non-deteriorated. Demographic factors such as time to start rt-PA and symptomatic/asymptomatic hemorrhage were not statistically different between the 2 groups. In the deteriorated group, mean age was higher, and NIHSS score and DWI volume were significantly larger than in the non-deteriorated group ($P < 0.05$). The DWI score and ASPECTS tended to be lower in the deteriorated than the non-deteriorated group but were not statistically different (Table). With a cutoff value of ≤ 7 , the DWI score could discriminate the deteriorated group from the non-deteriorated group with sensitivity of 50% and specificity of 87.5% and ASPECTS, with sensitivity of 50% and specificity of 81.2%. However, using DWI volume, sensitivity was 83.3% and specificity, 68.7% with a cutoff value of ≥ 20 mL (Fig. 2).

We found no correlation between DWI score, ASPECTS, or DWI volume and NIHSS ($r = -0.28$, -0.23 , and -0.39 ; $P = 0.20$, 0.28 , and 0.06 ; Spearman's test). In contrast, we found weak, but significant correlations between the DWI score or ASPECTS and DWI volume ($r = -0.80$ and -0.76 ; $P < 0.01$ and 0.01 ; Spearman's test).

Patients with low DWI score and ASPECTS tended to have largely varying DWI volumes; small

DWI volume reflected large variation in DWI score and ASPECTS (Fig. 3).

Discussion

ASPECTS is a unique system for evaluating acute ischemic change and is easily adapted even in emergency situations. A dichotomy of ASPECTS between 0 to 7 and 8 to 10 has been previously validated on noncontrast CT and shown to have a role in predicting prognosis of patients with acute stroke who have been treated with intravenous rt-PA within 3 hours after stroke onset.^{7,9} However, the ability of ASPECTS to predict patient outcome on DWI as well as on CT has not been confirmed. Barber and associates reported that ASPECTS values on DWI were lower than those on CT because of the higher sensitivity of DWI than CT in detecting acute ischemic lesion.¹⁰ In this study, ASPECTS lower than 8 points in 3 of 16 patients in the non-deteriorated group reflected that DWI as compared with CT can overestimate lesion extent. In contrast, DWI scores less than 8 in 2 patients suggested that the 11-point system that adds a region of white matter to the original 10 regions in ASPECTS can compensate for the overestimation on DWI, although we failed to find statistical significance between DWI and ASPECT scores. In addition, the overlap in DWI scores between the 2 patient groups was comparable or smaller when compared to the DWI volume, which showed a

Table. Patients treated with recombinant tissue plasminogen activator (rt-PA)

	Non-deteriorated group (n = 16)	Deteriorated group (n = 6)	P-value
Mean age (years)	69.8(45–82)	80.0(71–88)	0.028
Gender (male : female)	12 : 04	2 : 04	
Occluded artery			
Internal carotid artery	1(6.3)	5(83.3)	
Middle cerebral artery	12(75.0)	1(16.7)	
Unknown	3(18.7)	0(0.0)	
Time to rt-PA (minutes)	80–179(142.6)	97–178(137.5)	0.743
Initial NIHSS score	6–20(11.5)	14–23(20.5)	0.010
NIHSS score after treatment	0–19(2.5)	14–40(40.0)	<0.001
Alberta Stroke Programme Early CT Score (ASPECTS)	6–10(9.0)	4–10(7.0)	0.055
Diffusion-weighted imaging (DWI) score	6–11(9.0)	4–11(7.5)	0.087
DWI volume (cc)	0–18.6(5.2)	0–30.6(11.8)	0.030
Recanalization	9(56.3)	1(16.6)	
Hemorrhage			
symptomatic	1(6.25)	1(16.6)	
asymptomatic	7(43.75)	2(33.3)	

* Age, time to rt-PA and DWI volume, values in parentheses indicate the average for each group.

* NIHSS, ASPECT score, and DWI score, values in parentheses show the median value.

* Occluded artery, recanalization, and hemorrhage, values in parentheses indicate percentage.

Fig. 2. The diffusion-weighted imaging (DWI) score, Alberta Stroke Programme Early Computed Tomography Score (ASPECTS), DWI volume, and initial National Institutes of Health Stroke Scale (NIHSS) score in patients with acute ischemic stroke. (a) DWI score and NIHSS; (b) ASPECTS and NIHSS; (c) DWI volume and NIHSS.

With a cutoff value of ≤ 7 , the DWI score overestimates 2 patients of the non-deteriorated group and ASPECTS, 3 patients, though these scores are not significantly different between the deteriorated and non-deteriorated groups. With a cutoff value of ≥ 20 mL, DWI volumes overlapped substantially between the 2 groups, although the difference between the two was significant. There were no significant correlations between the 3 imaging scores and the NIHSS score.

Fig. 3. Correlation between diffusion-weighted imaging (DWI) scores or Alberta Stroke Programme Early Computed Tomography Score (ASPECTS) and DWI volume. **(a)** DWI score and DWI volume; **(b)** ASPECTS and DWI volume.

There are weak negative correlations between DWI score or ASPECTS and DWI volume ($P < 0.01$; Spearman's test). There was a tendency that patients with small DWI score had large variation of DWI volume, and patients with small DWI volume showed large variation of DWI score.

Fig. 4. A patient belonging to the non-deteriorated group (67-year-old woman with left M1 occlusion). **(a)–(c)** Initial magnetic resonance (MR) imaging after 1 hour and 15 min from symptom onset **(d)–(f)** Second MR imaging after 7 hours from onset. **(a), (b)** Diffusion-weighted imaging (DWI) showed slightly hyperintense area in left white matter and insula. Initial DWI score was measured to 9 points, and DWI volume was 47.2 cc. **(c)** Initial MR angiography (MRA) showed left M1 occlusion. After injection, symptoms disappeared rapidly and National Institutes of Health Stroke Scale (NIHSS) score improved from 20 to 0 points. **(d), (e)** Hyperintensity area on DWI still remained on left insula and a small area of high intensity in the white and gray matter, but the lesion did not spread. **(f)** Recanalization was confirmed by a second MRA. After 2 days, small hypointense lesions appeared within ischemia on T_2^* -WI, but these signal changes did not relate to her symptoms (not shown).

substantial overlap. Hence, DWI score can be utilized to predict patient outcome presumably more accurately than other methods when MR imaging is chosen for initial evaluation of patients with acute stroke.

Several issues remain with the DWI score. Our results showed no significant difference between DWI and original ASPECT scores. Further investigation with a larger number of patients is needed to determine an advantage of DWI score over ASPECTS. We should also confirm whether the corona radiata is appropriate as a region for evaluation and whether another region is needed to improve results. Neither was there a consensus as to whether small or faint ischemic lesion is counted and the non-eloquent regions, such as the insula, caudate nucleus, and temporal lobe, should be scored equally with the eloquent regions, such as the corona radiata and internal capsule. Further, similarly to ASPECTS, the DWI score is utilized only in the MCA area and cannot be applied to other areas.

Though there was no correlation between the

DWI score, ASPECTS, or DWI volume and NIHSS, most patients with higher initial NIHSS scores were classified into the deteriorated group whether MR imaging findings were good. Higher NIHSS would be an important parameter for predicting prognosis.

In our case, 11 of 22 patients (50%) showed areas of hypointensity on T_2^* -WI after rt-PA therapy, but most were asymptomatic and in only 2 patients was this related to their symptoms. We felt this signal change showed not only hemorrhage, but also small leakage of blood product from the vessels as a result of their high detectability. However, because our number of patients was small, we think it is difficult to evaluate if these scores can predict the hemorrhagic change.

Finally, our study has several limitations. First, the follow-up period was short. Though we evaluated prognosis at 24 hours after treatment, some cases were recanalized after 24 hours. We guessed that these patients might have improved long-term outcome, and evaluation might be better conducted after a longer period. However, because most

Fig. 5. A patient in the deteriorated group (81-year-old woman with left internal carotid artery [ICA] occlusion). (a)–(c) Initial magnetic resonance (MR) imaging after 1 hour from symptom onset. (d)–(f) Second MR imaging after 23 hours from onset. (a), (b) Faint area of hyperintensity on diffusion-weighted imaging (DWI) is shown in left temporal lobe (deep to subcortical white matter and along external capsule). Initial DWI score was measured at 9 points, and DWI volume was 25.3 cc. (c) Initial MR angiography (MRA) showed left ICA occlusion. Though her age was advanced, intravenous recombinant tissue plasminogen activator (rt-PA) thrombolysis was given after informed consent. (d)–(f) The hyperintense lesion on DWI was spread to the left anterior-temporal lobe, and the ICA occlusion was unchanged. The patient died after 2 days.

patients had moved to another hospital after intensive treatment in the acute phase, follow-up in the chronic phase was difficult. Second, our number of patients was small, and six of 22 had ICA occlusion, a condition generally known to have poor prognosis; this uneven distribution might bias prognosis. By increasing patient number and extending follow-up time, the DWI score might be demonstrated more useful to evaluate acute ischemic lesion. Third, our use of a 3T MR imaging scanner provided better detection of ischemic lesion than possible at 1.5T, but higher detectability may result in overestimation of the extent of ischemic lesion on DWI. Use of a high magnetic field also reduces examination time, but we should pay attention to other differences in using high magnitude MR imaging.

Conclusion

The semiquantitative DWI score modified from ASPECTS could distinguish with relatively high specificity patients with deteriorated NIHSS from those without deterioration. This method can be used to evaluate extent of acute ischemic lesion on DWI and may predict more accurately than ASPECTS or DWI volume patient outcome after thrombolytic therapy.

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