Acta Med. Okayama, 2016
Vol. 70, No. 4, pp. 237–242

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Original Article

The Usefulness of CT-Diffusion Weighted Image Mismatch in Patients with Mild to Moderate Traumatic Brain Injury

Kyohei Kin[a,b]*, Yasuhiro Ono[a], Takeshi Fujimori[a], Satoshi Kuramoto[a], Atsushi Katsumata[a], Yuji Goda[a], and Masamitsu Kawauchi[a]

[a]*Department of Neurosurgery, Kagawa Prefectural Central Hospital, Takamatsu 760–8557, Japan,*
[b]*Department of Neurological Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700–8558, Japan*

Traumatic brain injury (TBI) has a complex and heterogeneous pathology. It is frequently difficult to predict the neurological deterioration of patients with TBI, and unpredictable change may occur even when TBI is mild to moderate. When computed tomography (CT) findings are considered to be inconsistent with the traumatic origin or with the neurological deterioration of patients observed on admission, magnetic resonance imaging (MRI) is employed based on the standards of our ethical committee. In this retrospective study, we compared CT and diffusion weighted imaging (DWI) of patients with mild to moderate TBI in the very acute phase. When the high-intensity lesions on DWI are larger than the high-density lesions on CT images, we defined the imaging finding as a 'CT-DWI mismatch'. Between January 2010 and December 2013, 92 patients were inspected using both CT and MRI at admission, and we detected a CT-DWI mismatch in 35 patients. CT-DWI mismatch was 92.6% (95% confidence interval 79.8–97.9) sensitive and 84.6% (95% confidence interval 79.3–86.3) specific for the prediction of enlargement of the hemorrhagic lesions on repeat CT. CT-DWI mismatch is considered to be useful as one of the predictors of the enlargement of hemorrhagic lesions in patients with mild to moderate TBI.

Key words: magnetic resonance imaging, diffusion-weighted imaging, traumatic brain injury, head computed tomography scan, mild head injury

Computed tomography (CT) is very useful for the diagnosis and treatment of traumatic brain injury (TBI) because of its availability and its ability to detect intracranial hemorrhage, the mass effect of space-occupying lesions, and bony fracture. In The Japanese Guidelines for the Management of Severe Head Injury, CT is recommended as the first line of neuroimaging study [1].

Magnetic resonance imaging (MRI) is more sensitive than CT for detecting abnormal lesions. However, MRI is not recommended as the first line of neuroimaging study for patients with TBI in the guidelines of the Japanese Society of Neurotraumatology for safety reasons [1], The American College of Radiology and the National Institute for Health and Care Excellence. On the other hand, for patients with mild to moderate TBI and with a stable general condition, MRI can provide the details of the head injury. The first purpose of taking MRI images is to exclude diseases other

Received September 24, 2015; accepted January 20, 2016.
*Corresponding author. Phone:+81–86–235–7813; Fax:+81–86–235–7814
E-mail:thekinkorea@yahoo.co.jp (K. Kin)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

than TBI. MRI can sometimes clarify the true causes of TBI including cerebrovascular disease, epileptogenic disease and general metabolic disease. The second purpose is to explain the dissociation between the neurological deterioration and the CT findings.

In patients with TBI, diffusion-weighted imaging (DWI) has been reported to detect diffuse axial injury and edema [2]. However, only a few studies have reported a comparison of CT and DWI in the acute phase of head trauma. In this retrospective study, we compared CT and DWI imaging of patients with mild to moderate TBI in the very acute phase and evaluated their usefulness.

This study was approved by the ethical committee of Kagawa Prefectural Central Hospital (approval number: 101). Instead of acquiring individual agreement, we acquired comprehensive agreement on the information disclosure page of our hospital according to the Helsinki Declaration. The patients' private information and personal identities were protected in this study.

Materials and Methods

Subjects were identified retrospectively from the population of patients with TBI admitted to our department from January 1, 2010 to December 31, 2013. Patients who fulfilled the following criteria were included: 1) a Glasgow coma scale (GCS) score at admission of 9 to 15; 2) CT and DWI were obtained at the time of arrival; 3) repeat CT was obtained on the day following admission.

CT was performed according to the standard department protocol on a 64-slice multi-detector scanner (Aquilion TSX-101A, Toshiba Medical Systems Corporation, Otawara, Japan). MRI was performed using a standard stroke protocol on a 1.5-T scanner (MAGNETOM Avanto, Siemens Medical Solution, München, Germany). DWI, fluid-attenuated inversion recovery (FLAIR), T2-weighted images (T2WI), T2*-gradient recalled echo (T2*GRE), and magnetic resonance angiography (MRA) were provided. Apparent diffusion coefficients (ADCs) were obtained when considered necessary.

First, we compared CT image at admission with DWI images for each patient. When high-intensity areas on DWI were more than 5 mm larger in the greatest dimension than the high-density areas on CT, the latter of which suggest hemorrhagic changes, or we detect high-intensity areas on DWI where high-density areas were not detected on CT, we defined the imaging finding as a 'CT-DWI mismatch'. The influence that the CT-DWI mismatch exerted on the clinical course and outcome were retrospectively analyzed. We also evaluated the change in ADCs where a CT-DWI mismatch was detected.

A new appearance or an increase of >6 ml or $>30\%$ from the baseline volume of the high-density lesions on repeat CT at the same location as that of the CT-DWI mismatch was defined as 'enlargement of the hemorrhagic lesions on repeat CT'. CT and MRI were reviewed by more than one neurosurgeon to assess for the presence of CT-DWI mismatch and enlargement of the hemorrhagic lesion on repeat CT. Differences in interpretation were resolved by consensus using a panel including an additional neurosurgeon. Outcomes were assessed at the time of discharge using the Glasgow Outcome Scale (GOS). 'Favorable outcome' was defined as a GOS of 4 (moderately disabled) or 5 (good recovery).

Statistical analysis was performed using SPSS ver. 20.0 software (SPSS, Chicago, IL, USA). For statistical analysis, Mann-Whitney's U test and Fisher's exact probability test were used, and $p<0.05$ was defined as significant. The sensitivity and specificity of the accuracy of CT-DWI mismatch for the prediction of enlargement of the hemorrhagic lesions on repeat CT were evaluated by comparing a repeat CT with the initial CT.

Results

During the period of this study, 377 patients with TBI whose GCS scores at admission ranged from 9 to 15 were admitted to our department, and initially studied using CT. They were 58.9 ± 26.0 years old, and 62.6% were men. Among them, 330 patients were admitted with a GCS score of 13-15, and 47 patients had a GCS score of 9-12. Craniotomy or external ventricular drainage was performed in 43 patients as a surgical intervention. At the time of discharge, 279 patients (74%) were classified as having a favorable outcome (Table 1).

MRI was obtained at the time of arrival in 92 patients (24.4%). The average time from initial CT to MRI was 61.4 min (range, 23 to 135). Because the

patients had neither severe extracranial injuries nor vital sign abnormalities, we could obtain their initial MRI information, and also compare the CT and MRI findings. In the backgrounds of the patients, there was no significant statistical difference between the group that had undergone MRI and the group that had not undergone MRI at the time of arrival regarding age, gender, GCS score at admission, surgical intervention, or outcome (Table 2).

In 35 patients (38%), we detected a CT-DWI mismatch. There was no significant statistical difference between the group with CT-DWI mismatch and the group without CT-DWI mismatch with regard to background (age, gender, GCS score at admission, and use of antiplatelet or anticoagulation drug) (Table 3).

In the group with CT-DWI mismatch, we detected enlargement of the hemorrhagic lesions on repeat CT in 25 (71.4%) of 35 patients. On the other hand, we detected enlargement of the hemorrhagic lesions on repeat CT in only 2 (3%) of 57 patients in the group without CT-DWI mismatch. Enlargement of the hemorrhagic lesions on repeat CT was detected in the group with CT-DWI mismatch with significantly higher frequency ($p < 0.01$). CT-DWI mismatch was 92.6% (95% confidence interval 79.8–97.9) sensitive and

Table 1 Background of patients with mild to moderate TBI

No. of cases	377
Median age (yrs.) ± SD	58.9 ± 26.0
Male	236 (62.6)
GCS at admission	
13–15	330 (87.5)
9–12	47 (12.5)
Surgical intervention	43 (8.8)
Patient outcome (Glasgow outcome scale)	
favorable outcome (GR/MR)	279 (74)
unfavorable outcome (SD/VS/D)	98 (26)

All results given as number of patients(%) unless otherwise stated.

Table 2 Comparison of background and clinical course beteween patients with MRI at arrival and patients without MRI at arrival

	MRI on arrival (+)	MRI on arrival (−)	*p* value
No. of cases	92 (24.4)	285 (75.6)	
Median age (yrs.) ± SD	62.9 ± 23.9	58.7±27.1	0.533†
Male	56 (60.9)	180 (63.2)	0.711††
GCS at admission			
13–15	78 (84.8)	252 (88.4)	0.367††
9–12	14 (15.2)	36 (12.6)	0.367††
Surgical intervention	7 (7.6)	36 (12.6)	0.257††
Patient outcome			
favorable outcome (GR/MR)	66 (71.7)	213 (74.7)	0.586††
unfavorable outcome (SD/VS/D)	26 (28.3)	72 (25.3)	0.586††

All results given as number of patients(%) unless otherwise stated.
†Mann-Whitney's *U* test; ††Fisher's exact test.

Table 3 Comparison of background between patients with CT-DWI mismatch and patients without CT-DWI mismatch

	CT-DWI mismatch (+)	CT-DWI mismatch (−)	*p* value
No. of cases	35 (38)	57 (62)	
Median age (yrs) ± SD	66.6 ± 22.3	61 ± 24.4	0.149†
Male	17 (48.6)	39 (68.4)	0.07††
GCS score at admission -cases			
13–15	28	50	0.376††
9–12	7	7	0.376††
Antiplatelet drug	6	12	0.789††
Anticoagulant drug	3	2	0.365††

All results given as number of patients(%) unless Otherwise stated.
†Mann-Whitney't *U* test; ††Fisher't exact test.

84.6% (95% confidence interval 79.3–86.8) specific for the prediction of enlargement of the hemorrhagic lesions on repeat CT. Among 35 patients who showed a CT-DWI mismatch, ADCs were obtained in 24 patients. Twenty patients (83.3%) showed a reduction in ADCs and 4 patients (16.7%) showed heterogeneous ADC patterns.

Surgical interventions were performed in 3 (8.6%) of 35 patients with CT-DWI mismatch and in 4 (7%) of 57 patients without CT-DWI mismatch. There was no significant difference between these 2 groups. All of these surgical interventions were performed based on CT findings. With regard to patient outcomes, 24 (68.6%) of 35 patients with CT-DWI mismatch showed favorable outcomes and 42 (73.7%) of 57 patients without CT-DWI mismatch showed favorable outcomes. There was also no significant difference between these 2 groups (Table 4).

Case illustration. A 76-year-old man fell from a stepladder and was taken to a nearby hospital. There, he was diagnosed with a traumatic subarachnoid hemorrhage (SAH) by brain CT. He had a GCS score of 14 and showed no other neurological deficit.

Two h after the injury, he was transferred to our hospital for further evaluation and treatment. We took CT (Fig. 1A, B) and MRI (Fig. 1C, D) images to rule out aneurysmal SAH. We found a new appearance of hematoma in the left frontal lobe (Fig. 1B arrowhead) and a high-intensity lesion in the right temporal lobe on DWI (Fig. 1C arrow). The high-intensity lesion in the right temporal lobe on DWI is considered to constitute a CT-DWI mismatch because the CT did not detect any high-density lesions in the right temporal lobe. The ADCs decreased where the CT-DWI mismatch was detected (Fig. 1D arrow). MRA did not show any vascular abnormalities, and we diagnosed the patient with traumatic SAH.

A repeat CT obtained on the following day showed a new appearance of intracerebral hematoma in the same region where the CT-DWI mismatch was detected (Fig. 1E arrow).

Discussion

CT is the first-line choice for the evaluation of TBI because it is readily obtainable and is the cornerstone of rapid diagnosis [3], and MRI is not recommended as the first-line choice in general. The principle reasons for this as described in the guideline [1] include the risk of scanning patients with certain indwelling devices or occult foreign bodies and the fact that limited equipment is available for managing patients in MRI rooms.

At our hospital, we treat many stroke patients, and we have established algorithms to ensure that no magnetic materials are contained in the patient's entire body. The general condition of patients with mild to moderate TBI is relatively stable. Therefore, we think it is safe to obtain MRI scans of patients with mild to moderate TBI if their general condition is stable.

MRI inspection equipment is well established experimentally and clinically, and it provides detailed information about anatomy and biophysical processes. DWI, diffusion tensor imaging, FLAIR, T2WI, T2* GRE, susceptibility-weighted imaging and magnetic resonance spectroscopy have been analyzed for their usefulness in TBI [2, 4–7].

A few studies comparing CT and DWI in the acute phase have been reported, and we found only three studies which compare CT and DWI performed within 72 h of admission [2, 8, 9]. In these reports, the two examinations (CT and MRI) were not necessarily performed at the same time on admission. Our study is

Table 4 Comparison of clinical course and outcome between patients with CT-DWI mismatch and patients without CT-DWI mismatch

	CT-DWI mismatch (+)	CT-DWI mismatch (−)	*p* value†
Enlargement of hemorrhagic lesion on repeat CT	25 (71.4)	2 (3.5)	< 0.01
Surgical intervention	3 (8.6)	4 (7)	1
Patient outcome			
favorable outcome (GR/MR)	24 (68.6)	42 (73.7)	0.638
unfavorable outcome (SD/VS/D)	11 (31.4)	15 (26.3)	0.638

All results given as number of patients(%) unless otherwise stated.
† Fisher's exact test.

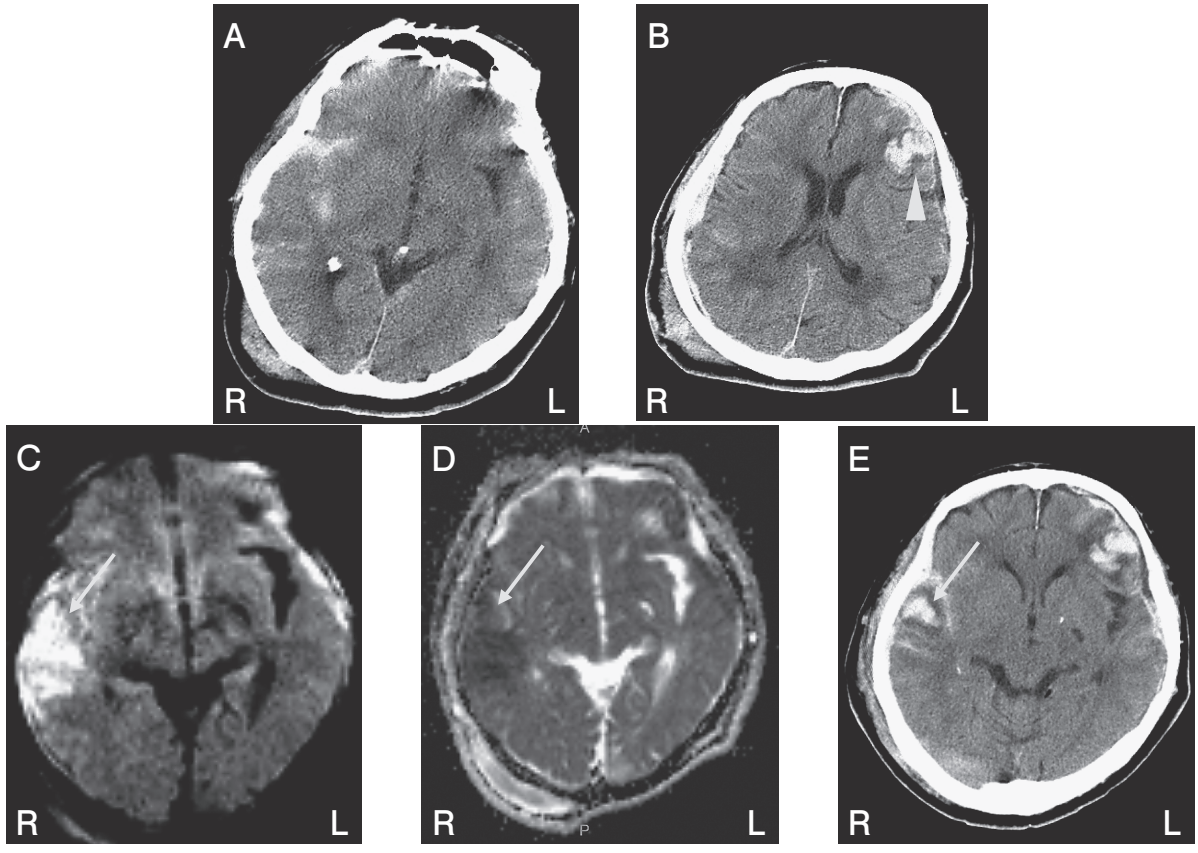

Fig. 1 Brain CT at the previous hospital revealed subarachnoid hemorrhage, but intracerebral hematoma was not detected. Repeat CT just after the patient was transferred to our hospital detected new appearance of hematoma in the left frontal lobe (**A** and **B** arrowhead) and a diffusion-weighted image revealed a high-intensity lesion in the right temporal lobe, which was considered to be a CT-DWI mismatch because CT did not detect high-density lesions in the right temporal lobe (**C** arrow). The ADCs decreased where the CT-DWI mismatch was detected (**D** arrow). Repeat CT obtained on the following day showed a new appearance of intracerebral hematoma in the same region where the CT-DWI mismatch was detected (**E** arrow).

the first examination comparing CT and DWI findings at the time of arrival.

Paszkowska *et al.* compared CT performed at the time of arrival and DWI performed within 24–72 h of the moment of injury in 8 patients with diffuse axial injury (DAI) and reported the usefulness of DWI for detecting DAI [2]. On the other hand, Manolakaki *et al.* compared CT and MRI performed within 48 h of onset and reported that MRI detected findings that were not detected using CT in some patients, but there were no changes in treatment because of these additional MRI findings. Finally, they concluded that early MRI was unnecessary because the information obtained using MRI did not affect the management of the patient [8].

In the present study, as in the report by Manolakaki *et al.*, the decision to perform surgical intervention was made based on CT findings. However, the finding of CT-DWI mismatch had high sensitivity and specificity with regard to predicting the enlargement of hemorrhagic lesions. The finding of CT-DWI mismatch should certainly not be the basis for performing a surgical intervention, but CT-DWI mismatch may predict the enlargement of hemorrhagic lesions which require surgical intervention. We cannot resolve how CT-DWI mismatch informs the decision to undergo surgical intervention because this is a retrospective study, and surgical interventions were performed in only a few patients. Further studies may provide more information. CT-DWI mismatch is definitely useful, however, to determine the timing of repeat CT and to assess the need for intensive and

careful observation.

There have been many studies on the topic of secondary insult after TBI, but no study has been able to directly explain the mechanism of the relationship between CT-DWI mismatch and the enlargement of hemorrhagic lesions. In our study, it is highly possible that cytotoxic edema occurred at the site where CT-DWI mismatch was detected because the ADCs decreased in the majority of cases. Ito *et al.* reported that cytotoxic edema occurred one h after head trauma in a TBI rat model [10], and this report supported our findings. Also, Thomale *et al.* reported that cortical hypoperfusion was found within the early phase following trauma and pericontusional blood flow was subsequently increased in a TBI rat model [11]. Based on this study, we infer that cytotoxic edema could be followed by vasodilatation because it is associated with ischemic change, and the vasodilatation following cytotoxic edema may be the cause of the enlargement of the hemorrhagic lesion. Further examination should be performed.

In conclusion, CT-DWI mismatch is useful as a predictor of the enlargement of hemorrhagic lesions and has the potential to have an impact on clinical decision-making. MRI is worth performing in patients with mild to moderate TBI if the patient's safety can be guaranteed.

Acknowledgments. We are deeply indebted to all the staff at Kagawa Prefectural Central Hospital.

References

1. Onuma T, Aruga T, Shima K, Abe T, Ogawa T, Okudera H, Ono J, Katayama Y, Kawai N, Kawamata T, Kohmura E, Sakaki T, Sakamoto T, Sasaki T, Sato A, Shiogai T, Shigemori M, Suzuki M, Takasato Y, Tokutomi T, Tomita H, Toyoda I, Nagao S, Nakamura H, Park YS, Matsumae M, Miki T, Miyake Y, Murai H, Yamaura A, Yamaki T, Yamada K, Yoshimine T, Araki T, Uzura M, Ohtani N, Okuno K, Karibe H, Kuroda Y, Sakakibara T, Suehiro E, Takayama Y, Tani S, Dohi K, Nakayama N, Nawashiro H, Maeda T, Miyagi T, Miyata A, Yagishita M and Yatsushige H: The Guidelines for the Management of Severe Head Injury, Ed3, JSNT Jpn Soc Neurotraumatol (2013): 25–33, 158–159.
2. Paszkowska E, Wasilewski G, Szalcunas-Olsztyn A, Jancewicz P and Stefanowicz E: The comparison of the value of ct imaging and selected MRI sequences (including DWI) in the evaluation of axonal injuries. Pol J Radiol (2010) 75: 13–17.
3. Haydel MJ, Preston CA, Mills TJ, Luber S, Blaudeau E and DeBlieux PM: Indications for computed tomography in patients with minor head injury. N Engl J Med (2000) 343: 100–105.
4. Rutgers DR, Toulgoat F, Cazejust J, Fillard P, Lasjaunias P and Ducreux D: White matter abnormalities in mild traumatic brain injury: a diffusion tensor imaging study. AJNR Am J Neuroradiol (2008) 29: 514–519.
5. Choi JI, Kim BJ, Ha SK, Kim SH, Lim DJ and Kim SD: Comparison of subgroups based on hemorrhagic lesions between SWI and FLAIR in pediatric traumatic brain injury. Childs Nerv Syst (2014) 30: 1011–1019.
6. Geurts BH, Andriessen TM, Goraj BM and Vos PE: The reliability of magnetic resonance imaging in traumatic brain injury lesion detection. Brain Inj (2012) 26: 1439–1450.
7. Moffett JR, Arun P, Ariyannur PS and Namboodiri AM: N-Acetylaspartate reductions in brain injury: impact on post-injury neuroenergetics, lipid synthesis, and protein acetylation. Front Neuroenergetics (2013) 5: 11.
8. Manolakaki D, Velmahos GC, Spaniolas K, de Moya M and Alam HB: Early magnetic resonance imaging is unnecessary in patients with traumatic brain injury. J Trauma (2009) 66: 1008–1012; discussion 1012–1004.
9. Mannion RJ, Cross J, Bradley P, Coles JP, Chatfield D, Carpenter A, Pickard JD, Menon DK and Hutchinson PJ: Mechanism-based MRI classification of traumatic brainstem injury and its relationship to outcome. J Neurotrauma (2007) 24: 128–135.
10. Ito J, Marmarou A, Barzo P, Fatouros P and Corwin F: Characterization of edema by diffusion-weighted imaging in experimental traumatic brain injury. J Neurosurg (1996) 84: 97–103.
11. Thomale UW, Schaser K, Kroppenstedt SN, Unterberg AW and Stover JF: Cortical hypoperfusion precedes hyperperfusion following controlled cortical impact injury. Acta Neurochir Suppl (2002) 81: 229–231.