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FULL PAPER

Use of multisequence 3.0-T MRI to detect severe traumatic brain injury and predict the outcome

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Objective: The aim of this study was to evaluate multisequence 3.0-T MRI in the detection of severe traumatic brain injury (sTBI) and in predicting the outcome.

Methods: 32 patients with sTBI were prospectively enrolled, and multisequence 3.0-T MRI was performed 4–8 weeks post injury. Quantitative data were recorded on each sequence. The ability to display the parenchymal lesions was compared with that of 64-slice spiral CT. The clinical and radiological results were correlated with the Glasgow Outcome Scale Extended scores 6 months after injury.

Results: 3.0-T MRI could display more lesions than CT, especially when the lesion was deeply located. The lesion volumes and diffuse axonal injury (DAI) scores were different between good and poor outcome groups on fluid attenuated inversion recovery ($p < 0.05$). The apparent diffusion coefficient (ADC) values of the splenium of the

corpus callosum and brain stem were also different ($p < 0.05$). Patients with unfavourable outcome showed a significantly higher volume of haemorrhage on susceptibility-weighted imaging than those with favourable outcomes and had haemorrhages generally located more deeply. Logistic regression analysis revealed that the location of haemorrhage and the ADC values of the splenium of the corpus callosum were independent risk factors for poor outcome, with an overall predictive accuracy of 91.4%.

Conclusion: The joint use of conventional and advanced sequences of 3.0-T MRI can comprehensively detect the pathological changes occurring after sTBI. Haemorrhagic and non-haemorrhagic DAIs in deep structures strongly suggest poor outcome.

Advances in knowledge: This article improves the understanding of advanced MRI sequences in the detection of patients with sTBI and prediction of prognosis.

INTRODUCTION

In modern society, traumatic brain injury (TBI) is the main cause of death and disability in young adults.¹ The mortality associated with severe TBI (sTBI) remains high, and even if the patient survives, TBI can result in profound neurological deficits.²

Before the invention of CT, clinical assessment of TBI had to rely on the patient's level of consciousness, pupillary response etc., as well as laboratory indicators and neurophysiological measures such as evoked potentials and electroencephalography. However, these are only indirect measures of the injury and are easily affected by drugs or the patient's general condition and associated injuries; thereby, they can lead to errors in clinical judgment.^{3–5} Radiological tests can help to intuitively and dynamically observe the intracerebral changes occurring after TBI without being affected by the above-mentioned factors and can provide valuable clinical guidance.

The sensitivity of CT scans is adequate to observe acute intracerebral haematoma or bone fracture, but it is not high enough to detect diffuse axonal injury (DAI),^{6–10} which is present in 90% of patients with sTBI and largely impacts their outcome.^{11,12} MRI is superior to CT in detecting DAI lesions.^{6–10,13,14} The high sensitivity to microlesions of MRI has great benefit to patients with TBI with different degrees of damage. For mild TBI [*i.e.* Glasgow Coma Scale (GCS) score of 13–15 on admission], MRI can detect the lesions responsible for their clinical symptoms, which are often not visible on CT scans. MRI can also discover the axonal damage that is often covered by mass lesions in moderate-to-severe TBIs. The advanced sequences are extremely sensitive to particular pathological changes and can also provide quantitative parameters. Diffusion-weighted imaging (DWI) can not only discriminate the type of brain oedema but also provide apparent diffusion coefficient (ADC) values that measure the water diffusion. Susceptibility-weighted imaging (SWI) has a

broad application in TBI because of the high sensitivity to microbleeding. Diffusion tensor imaging (DTI) can produce quantitative data about white matter tracts and make it more intuitive after processing. To date, use of multisequence MRI in patients with TBI has aroused growing attention from researchers.^{15,16} We hypothesized that the joint use of MRI sequences could comprehensively detect intracerebral injuries occurring after TBI and improve the accuracy of prognosis.

METHODS AND MATERIALS

Patient selection

The institutional review board of Shanghai Jiao Tong University Affiliated Sixth People's Hospital approved this study. We prospectively enrolled patients with closed sTBI (GCS <8 on admission) treated in our hospital between October 2010 and May 2012. Exclusion criteria were (1) a history of neurological disorders or previous brain injury, (2) drug or alcohol abuse, (3) missile brain injury, (4) physiological instability or contraindication to MRI and (5) if refused by the family members. The MRI scans were performed 4–8 weeks post injury, when the patients' vital signs were stable and they could tolerate the transport and test. Written informed consent was obtained from all participants' representatives. 113 patients with sTBI were admitted in this period, and 63 of them were excluded, mainly owing to Criteria 4 and 5 (49 patients). Another 15 patients were excluded because of motion artefacts. A specialized neurosurgeon (LY) administered the test and closely observed the condition of every patient. Appropriate sedation (diazepam injection, 10 mg, intravenously) was used with intensive care when the patient could not co-operate satisfactorily. MRI scans were obtained from 35 patients (28 males and 7 females; mean age, 46 ± 13 years) who met all eligibility criteria. The following clinical information was also recorded: age, gender, cause of injury, GCS score (recorded as the lowest observed after admittance or before intubation or sedation in cases of pre-hospital intubation or sedation) and pupil response in the emergency room (ER), additional injuries and neurosurgical intervention if any. Combined injuries were assessed by injury severity score.¹⁷ 22 age-matched control subjects (16 males and 6 females; mean age, 42 ± 18 years) were also examined at the same time. They were outpatients who had no known history of central nervous system disease or trauma and who volunteered to participate in this study with informed consent. Their MRI scans were completely normal upon repeated reviews.

Imaging protocols

MRI was performed with a 3.0-T Verio Siemens scanner (Erlangen, Germany) equipped with an eight-channel head coil. The following sequences were used: (1) axial T_1 weighted scan [repetition time (TR)/echo time (TE), 2000/9 ms]; (2) axial T_2 weighted imaging (TR/TE, 6000/95 ms); (3) axial fluid attenuated inversion recovery (FLAIR) [TR/TE, 8500/94 ms; field of view (FOV), 230×220 mm; matrix, 256×180 pixels]; (4) DWI (TR/TE, 5400/94 ms; FOV, 229×229 mm; matrix, 162×162 pixels; b -values, 0, 1000 s m^{-2} ; section thickness, 6 mm with an intersection gap of 1.8 mm) and (5) axial SWI (TR/TE, 36/15 ms; FOV, 220×220 mm; matrix, 384×384 pixels; flip angle, 6° ; section thickness, 2 mm with an intersection gap of 0 mm). The total scan time was approximately 8 min.

The first CT scan after admission or the first follow-up scan after surgery was used for comparison, using a 64-slice spiral CT scanner (GE Healthcare, Milwaukee, WI), and classified using the modified Marshall score¹⁸ (YL, with 20 years' experience, and XW, with 9 years' experience): (1) Category I: no visible pathological component; (2) Category II: high or mixed density contusions ≤ 25 ml, visible base cisterns and brain shift ≤ 5 mm; (3) Category III: high or mixed density contusions ≤ 25 ml, compressed or obliterated base cisterns, and brain shift ≤ 5 mm; (4) Category IV: high or mixed density contusions ≤ 25 ml, compressed or obliterated base cisterns, and brain shift > 5 mm; and (5) Category V: any mass > 25 ml that was not surgically evacuated. Our principle of classification was based on the lesion burden; therefore, the original Category V "any mass lesion that was surgically evacuated" was discarded.

MRI analysis

Original data were transmitted to a Siemens Syngo® fastView work station (Erlangen, Germany), and images were evaluated by two experienced neuroradiologists (YL and XW) who were both blinded to the clinical situation. Intraparenchymal lesions were defined as foci of isointensity to hypointensity on T_1 weighted imaging (T1WI) and hyperintensity on T_2 weighted imaging (T2WI), FLAIR,¹⁹ and extra-axial lesions were not included. Hypointense foci, other than vascular structures or calcifications, on SWI were defined as traumatic haemorrhage.^{20,21} The volume of lesion and haemorrhage was calculated according to the ellipsoid method:²² $\text{volume} = 4/3\pi \times 0.5a \times 0.5b \times 0.5c$, where a corresponds to the largest lesion diameter, b corresponds to the largest perpendicular lesion diameter and c corresponds to the slice thickness times the number of slices that the lesion appears on. The location/extent of the lesion or haemorrhage was classified by the DAI score: (0) no visible lesions; (1) grey/white matter only; (2) corpus callosum $\pm$ grey/white matter; (3) brain stem (BS) $\pm$ grey/white matter; (4) grey/white matter + corpus callosum + BS.

The ADC map was automatically generated by the work station, and 12 regions of interest (ROIs) were manually drawn in the predilection areas of DAI,²³ and their ADC values were recorded (Figure 1). The ROIs included the following structures: bilateral centrum semiovale (CS), genu, body and splenium of the corpus callosum (CCS) and BS.

Outcome assessments

Neurological function was assessed at 6 months by two neurosurgeons (SC and LY) using the Glasgow Outcome Scale Extended (GOSE) and was dichotomized into poor (GOSE 1–5, $n = 19$) and good (GOSE 6–8; $n = 16$) outcomes.

Statistical analysis

Quantitative data were expressed as the mean $\pm$ standard deviation and compared using Student's t -tests. Non-parametric tests were used to compare categorical variables (Marshall CT score, DAI score, location of haemorrhage). Spearman rank correlation coefficients (r) were calculated to evaluate the strength of the associations between clinical radiological predictors and the outcome variable. A multiple logistic regression mode with stepwise selection was built to identify independent

Figure 1. Axial apparent diffusion coefficient (ADC) maps including 13 regions of interest selected for quantitative analysis of ADC values: 1, centrum semiovale; 2, body of the corpus callosum; 3, genu of the corpus callosum; 4, splenium of the corpus callosum; and 5, brain stem.

predictors of poor outcome. The regression model included the clinoradiological variables associated with an unfavourable outcome in univariate analysis. The results of regression analysis are reported as the odds ratio (OR) and 95% confidence intervals (CIs). Differences were considered significant at p -values <0.05 . Statistical analysis was performed using the SPSS® program v. 19.0 (IBM SPSS Inc., Chicago, IL).

RESULTS

Patient characteristics

The clinical data of 35 patients are summarized in [Table 1](#). There were 28 male and 7 female patients whose ages ranged from 17 to 70 years, with a mean age of 45.7 ± 13.0 years. Most patients (74%) were injured in traffic accidents. 3 patients (9%) were involved in falls, and 6 patients (17%) could not provide details. 14 patients (40%) had a GCS of 3–5 at admission, and the others had a GCS of 6–8. 10 patients (29%) had at least 1 fixed dilated pupil, and 13 patients had additional (extracranial) injuries, most of which were limb fractures or facial contusion. The elapsed time from injury to MRI ranged from 26 to 58 days (mean, 37 days). Emergency operations were performed in 21 patients (60%). Representative images from 2 patients with different outcomes are shown in [Figures 2 and 3](#).

Imaging findings

Three patients showed no visible parenchymal lesions on CT (modified Marshall CT score of Category I), 18, 6, 3 and 5 patients had Category II, III, IV and V, respectively. Only 3 patients had corpus callosum lesions, and BS lesions were detected in another 2 patients. A significantly larger number of lesions were detected by 3.0-T MRI, and all patients had parenchymal lesions, with 13, 8, 8 and 6 patients having grade 1, 2, 3 and 4 DAI scores, respectively; thus, 14 patients had lesions of the corpus callosum, and 14 patients had BS injury. SWI detected traumatic haemorrhage in 31 patients (89%). Only 4 patients showed lesions on conventional MRI (cMRI), with SWI being negative for haemorrhage, indicating non-haemorrhagic axonal injury. The location of the haemorrhagic lesions was as follows: 11 (31%) were located in grey/white matter or the cerebellum, 14 (4%) were at the corpus callosum and 15 (43%) were at the BS. The ADC values of the ROIs of patients with TBI and controls are listed in [Table 2](#). The ADC values of the TBI group were significantly higher than those of the control group in all predilection areas, which suggests the presence of axonal injury or oedema in these areas. The imaging results between different outcome groups are shown in [Table 3](#). Patients with poor outcome had a significantly larger volume of traumatic lesions on FLAIR and located more deeply (larger DAI scores). The ADC values of the CCS and BS were also higher in patients with

Table 1. Clinical data on 35 adult patients with severe traumatic brain injury

Number	Age (years)	Sex	Cause of injury	Glasgow Coma Scale in the emergency room	Pupil ^a	Combined injury	Surgery	Days to MRI	Glasgow Outcome Scale Extended
1	25	M	MVA	3	2	Y	Y	38	7
2	56	F	MVA	8	2	Y	Y	39	6
3	63	M	Unknown	5	1	N	Y	26	6
4	30	M	Unknown	6	2	N	Y	29	8
5	36	M	MVA	8	2	Y	Y	30	6
6	70	M	MVA	5	1	N	Y	41	1
7	37	M	Fall	5	2	Y	Y	27	2
8	43	F	MVA	7	1	N	Y	29	7
9	52	M	MVA	7	2	N	N	40	6
10	40	M	Unknown	5	2	N	N	40	1
11	37	M	MVA	7	1	N	Y	37	4
12	51	F	Unknown	6	2	Y	N	29	6
13	17	M	MVA	3	1	N	Y	38	7
14	37	M	MVA	5	1	N	N	41	6
15	25	M	MVA	5	1	Y	Y	38	2
16	65	F	MVA	7	2	N	N	29	1
17	57	M	MVA	7	2	N	Y	32	1
18	42	M	MVA	5	2	N	N	41	6
19	48	M	MVA	8	2	Y	Y	30	1
20	59	M	MVA	4	2	N	Y	35	1
21	39	F	MVA	7	2	Y	N	27	6
22	51	M	MVA	7	2	Y	N	41	6
23	40	M	MVA	6	2	Y	N	36	7
24	61	M	MVA	6	2	N	Y	47	1
25	54	F	MVA	7	2	N	N	29	8
26	32	M	MVA	5	1	N	Y	30	3
27	55	M	MVA	6	2	Y	N	55	3
28	45	M	MVA	6	2	Y	N	45	6
29	34	M	Unknown	5	2	N	N	34	6
30	32	F	MVA	7	2	N	Y	45	6
31	48	M	Fall	7	2	N	Y	32	4
32	58	M	Fall	4	1	N	Y	58	5
33	39	M	Unknown	5	1	N	Y	58	4
34	56	M	MVA	8	2	N	N	39	6
35	66	M	MVA	6	2	Y	Y	56	5

^aPupil reaction: 1 means at least one side of fixed dilated pupil and 2 means normal on both sides.

F, female; M, male; MVA, motor vehicle accident; N, no; Y, yes.

Figure 2. Imaging from a 54-year-old female patient who was injured in a car accident and had a Glasgow Coma Scale score of 7 upon arrival at our emergency room. She remained in a coma for 4 days and was discharged after 20 days. She was mildly disabled at discharge but achieved full recovery at 6 months. Axial T_1 weighted imaging [repetition time (TR)/echo time (TE), 2000/9 ms] fluid attenuated inversion recovery (FLAIR) [TR/TE, 8500/94 ms; field of view (FOV), 230×220 mm; matrix, 256×180 pixels], and susceptibility-weighted imaging (SWI) (TR/TE, 36/15 ms; FOV, 220×220 mm; matrix, 384×384 pixels; flip angle, 6°) images are shown at three levels of the brain. There are no visible lesions on T_1 and FLAIR images, and only two traumatic microhaemorrhagic lesions in the right temporal lobe and peritrigonal grey matter (arrows) on SWI.

unfavourable outcomes, and the haemorrhagic lesions were also larger and deeper in these patients.

Correlations between clinoradiological data and outcome

The correlations between clinoradiological results and outcome are shown in Table 4. The clinical variables were not correlated with the GOSE score 6 months post injury, except for

age. Among the radiological variables, the DAI score, lesion volumes on FLAIR, ADC values of the CCS and BS, and volume and location of the haemorrhagic lesions on SWI were significantly correlated with the outcome.

Multivariate logistic regression analysis

Variables that correlated with the outcome in the univariate analysis were further analysed using the multivariate logistic regression

Figure 3. Imaging from a 70-year-old male patient who was injured in a car accident and had a Glasgow Coma Scale score of 5 upon arrival at our emergency room. He remained in a coma until he died 6 months later. Axial T_1 weighted imaging (TR/TE, 2000/9 ms), fluid attenuated inversion recovery (FLAIR) [repetition time (TR)/echo time (TE), 8500/94 ms; field of view (FOV), 230×220 mm; matrix, 256×180 pixels], and susceptibility-weighted imaging (TR/TE, 36/15 ms; FOV, 220×220 mm; matrix, 384×384 pixels; flip angle, 6°) images are shown at three levels of the brain. There are large hyperintense lesions on FLAIR images, indicating residual brain damage and brain ischaemia. Numerous traumatic microhaemorrhagic lesions can also be observed in the left temporal lobe, brain stem and corpus callosum (arrows).

model. The results showed that the ADC_{ccs} [OR = 5.219 (95% CI, 1.528–20.622), $p = 0.01$] and the location of the haemorrhagic lesions [OR = 9.63 (95% CI, 2.437–38.057), $p < 0.001$] were independent risk factors for poor outcome, with an overall predictive accuracy of 91.4%, whereas the other factors could not be used to predict the outcome.

DISCUSSION

The prognosis of patients with TBI, especially the ones with sTBI, varies significantly.⁴ This article has focused on the actual brain tissue injury, which is a direct reflection of brain trauma. The findings suggest that the combination of DWI and SWI can improve the accuracy of predicting the outcome in patients with sTBI.

Table 2. Apparent diffusion coefficient (ADC) values of regions of interest (ROIs) between the traumatic brain injury (TBI) group and the control group

ROIs	ADC values ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)		<i>p</i> -value
	TBIs (<i>n</i> = 35)	Controls (<i>n</i> = 22)	
ADC _{cs}	0.959 $\pm$ 0.057	0.922 $\pm$ 0.522	0.02 ^a
ADC _{cgg}	0.651 $\pm$ 0.043	0.624 $\pm$ 0.052	0.04 ^a
ADC _{ccb}	0.770 $\pm$ 0.056	0.724 $\pm$ 0.069	0.04 ^a
ADC _{ccs}	0.740 $\pm$ 0.080	0.681 $\pm$ 0.060	0.005 ^a
ADC _{bs}	0.760 $\pm$ 0.066	0.698 $\pm$ 0.049	<0.001 ^a

^aSignificant compared with controls at $p < 0.05$ using the Student's *t*-test.

bs, brain stem; ccb, body of corpus callosum; cgg, genu of corpus callosum; ccs, splenium of corpus callosum; cs, centrum semiovale.

The lesion burden of the parenchyma reflects the severity of the injury.²⁴ Chastain et al⁶ have found that T2WI and FLAIR can detect more lesions than CT and can consistently discriminate between patients with good and poor outcomes. Other studies have also demonstrated that MRI is superior to CT in detecting residual brain damage at the subacute or chronic stage of TBI.^{7–11} The injuries shown by MRI mainly consist of local contusions and secondary changes, such as oedema and ischaemia, which appeared as hypointensities on T1WI and hyperintensities on T2WI and FLAIR. The cerebrospinal fluid often interferes with the ability to detect hypointensities on T1WI and T2WI and influences the interpretation of lesions. Therefore, we used FLAIR to detect residual lesions and found that it correlated with the outcome ($r = -0.501$). This finding contradicts the results of some previous studies, which did not find any relationship between the results of cMRI and the outcome.^{9,25} These differences can presumably be explained by the superior resolution of the 3.0-T MRI or the differences in patient populations. We rated the location and extent of the lesions by the DAI score and found that the prognosis was worse when the lesions were located deeper, consistent with the Ommaya–Gennarelli model.^{26–28}

DAI is a type of shearing lesion that occurs as a result of acceleration–deceleration or rotational force, and is typically located in the long white matter fibre tracts such as the grey–white matter interface, corpus callosum and upper BS.^{19,29} The pathological change of DAI is characterized as a break in the axonal membrane, leading to misaligned axons and axonal retraction balls.³⁰ Different degrees of DAI have been shown to be present in 80–90% of patients with sTBI, and their extent greatly influences the prognosis.¹¹ DAI is often invisible on CT scans and appears as scattered focal lesions on cMRI. However, the magnitude of DAIs is often underestimated, which has been proved by the discrepancy between cMRI findings and outcomes in some patients with TBI.^{6,31} The clinical application of high-field (3.0-T) MRI and the use of advanced sequences that are sensitive to different pathological changes make it possible to comprehensively detect DAI.

DWI detects the random thermal movement (Brownian motion) of water molecules in tissues and was originally used to demonstrate brain oedema occurring after brain ischaemia or stroke.³² The mean rate of water diffusion in the pre-selection area refers to ADC values, and it makes the DWI able to

Table 3. Comparison of imaging results in different outcome groups

Radiological variables	Good outcome (<i>n</i> = 19)	Poor outcome (<i>n</i> = 16)	<i>p</i> -value
Marshall CT score	2.37 $\pm$ 1.17	3.06 $\pm$ 1.18	0.1
Lesion volume on fluid attenuated inversion recovery (ml)	13.14 $\pm$ 4.76	25.01 $\pm$ 7.74	<0.001 ^a
Diffuse axonal injury score	1.53 $\pm$ 0.77	3.00 $\pm$ 0.97	<0.001 ^a
ADC _{cs} ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	0.952 $\pm$ 0.458	0.967 $\pm$ 0.068	0.42
ADC _{cgg} ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	0.663 $\pm$ 0.050	0.637 $\pm$ 0.029	0.08
ADC _{ccb} ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	0.760 $\pm$ 0.043	0.776 $\pm$ 0.097	0.1
ADC _{ccs} ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	0.697 $\pm$ 0.072	0.790 $\pm$ 0.059	0.009 ^a
ADC _{bs} ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$)	0.734 $\pm$ 0.075	0.791 $\pm$ 0.036	<0.001 ^a
Location of haemorrhage	1.11 $\pm$ 0.81	3.38 $\pm$ 0.89	<0.001 ^a
Volume of haemorrhage (ml)	3.40 $\pm$ 2.99	5.98 $\pm$ 2.17	0.007 ^a

ADC, apparent diffusion coefficient; bs, brain stem; ccb, body of corpus callosum; cgg, genu of corpus callosum; ccs, splenium of corpus callosum; cs, centrum semiovale.

^aSignificant difference between poor outcome and good outcome at the $p < 0.05$ level using Student's *t*-test or Mann-Whitney test.

Table 4. Correlation between clinical/radiological factors and outcome

Clinicoradiological variables	GOSE score 6 months post injury	
	<i>r</i> -value	<i>p</i> -value
Age (years)	−0.431	0.01 ^a
Sex	0.18	0.29
Cause of injury	−0.01	0.95
Glasgow Coma Scale score in the emergency room	0.023	0.9
Pupil	0.03	0.87
Surgery	0.229	0.19
Combined injury	−0.105	0.55
Marshall CT score	−0.282	0.1
Diffuse axonal injury score	−0.501	0.002 ^a
Lesion volume on fluid attenuated inversion recovery	−0.485	0.003 ^a
ADC _{cs}	0.054	0.76
ADC _{cgg}	0.335	0.06
ADC _{ccb}	0.244	0.15
ADC _{ccs}	−0.629	<0.001 ^a
ADC _{bs}	−0.739	<0.001 ^a
Location of haemorrhage	−0.857	<0.001 ^a
Volume of haemorrhage	−0.560	<0.001 ^a

ADC, apparent diffusion coefficient; bs, brain stem; ccb, body of corpus callosum; cgg, genu of corpus callosum; ccs, splenium of corpus callosum; cs, centrum semiovale; GOSE, Glasgow Outcome Scale Extended.

^aSignificant correlation between clinicoradiological variables and GOSE score 6 months post injury at $p < 0.05$ using Spearman rank correlation coefficients.

distinguish between vasogenic and cytotoxic oedema by their different diffusion patterns:³³ high diffusion because of the increased permeability in vasogenic oedema (increased ADC value) and low diffusion because of the narrowed extracellular space in cytotoxic oedema (decreased ADC value). On the other hand, diffusion changes after brain oedema occur much earlier than the changes detected on FLAIR.³³ Previous studies suggest that changes of ADC values in the corpus callosum and BS are associated with the outcomes.^{23,34,35} We quantitatively tested the water diffusion in the predilection areas of DAI (CS, corpus callosum and BS) and found that the increased ADC values in patients with TBI were comparable to those in the control subjects, which can be explained by the compromised obstruction of the broken axonal membrane, or they may be due to residual oedema. The ADC values in the CCS and BS were significantly increased in patients with unfavourable outcomes, and the ADC_{ccs} proved to be an independent risk factor for poor prognosis. These findings indicate that traumatic axonal injury in these areas has a great impact on prognosis, which is consistent with previous reports.

SWI was recently developed and first used in venography.³⁶ It uses the paramagnetic properties of intravascular deoxy-haemoglobin and methaemoglobin or haemosiderin to visualized haemorrhages with extremely high sensitivity, which makes it the best currently available tool to detect haemorrhagic

DAIs.^{37–39} Studies using SWI in evaluating patients with TBI are relatively rare, and the available data suggest that SWI is superior to gradient echo sequence or CT in detecting traumatic microbleeds.^{20,21,37,39,40} However, there is some controversy about its prognostic value, mainly owing to the high false-positive rate because of its high sensitivity.²¹

In the present study, we used SWI and carefully interpreted the adjacent slices to exclude vascular structures, ruling out lesions that could not be easily distinguished from small veins—a method recommended by Barnes and Haacke.³⁶ Previous studies based on cMRI have found that most DAI lesions are non-haemorrhagic,^{7,24,41,42} but with the advent of SWI, this theory has been questioned.^{39,43} In this study, intraparenchymal haemorrhages were found in 88.6% of patients with sTBI and the volume of haemorrhage correlated with the outcome. The location of haemorrhagic lesions was also deeper in patients with poor prognosis, which was also an independent risk factor for poor outcome, with an overall predictive accuracy of 91.4%, combined with the ADC_{ccs}. It is worth noting that 11 of 15 patients with BS microbleeds had an unfavourable outcome. However, two patients who had a GCS of 3 and bilateral mydriasis in the ER (emergency CT scans showed large acute epidural haematoma and brain herniation) had a good outcome after neurosurgical intervention, and their SWIs were also negative for haemorrhages in deep structures. These uncommon

cases indicate that assessments solely relying on clinical manifestation (*i.e.* GCS score) have limitations, and the observation of haemorrhagic lesions in critical areas contributes greatly to determining the prognosis of patients with TBI.

Owing to the more serious condition (60% of patients required surgery), we carry out the examination at 4–8 weeks after injury, which is later than in previous studies (mostly at 2–4 weeks). In order to lower the risk during transport, we postpone MRI until patients are sufficiently stable; and this may impact the results: the haemorrhagic lesions, especially microbleeds, may have been absorbed and the extent of gliosis or malacia increased, thus changing the volume of lesions and haemorrhages. On the other hand, the brain oedema has further subsided, which reduces the interference.

There are still several limitations to our study. For example, the relatively small sample size may have affected the precision of the logistic regression analysis. In addition, the interpretation of the results is also limited by the lack of follow-up of MRI examinations in all patients, which hinders our understanding of the pathological progress. Moreover, this study mainly included patients with stable vital signs who could tolerate the test, but many patients with sTBI are still in a critical condition 4–6 weeks

post injury; thus, the results are affected by selection bias and have been shifted towards a better outcome. Furthermore, haemorrhagic lesion volume was measured in a semi-quantitative way, resulting in greater errors when there were a large number of small lesions. In order to reduce the risk and the amount of sedation, we did not perform the DTI sequence that needs a relatively long time. The sensitivity of the fibre track of this technology has been confirmed, which makes it a promising tool for DAI detection. We are now conducting related animal experiments and the results will be used in our patients in further research.

In conclusion, none of the single MRI sequences can detect all of the pathological changes occurring after TBI; however, the combined use of advanced sequences makes it possible to detect the overall intracranial pathological changes after TBI. Significant results have been achieved using this approach, primarily in animal studies.⁴⁴ Clinical investigations have been relatively rare, but promising results have already been obtained, showing that the combined use of multiple sequences has a larger prognostic value than the use of a single sequence.^{15,16} The present study also demonstrates that axonal injury, especially haemorrhagic injury at the critical sites, greatly affects the prognosis and that the combined use of DWI and SWI improves the accuracy of prediction in patients with sTBI.

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