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RESEARCH ARTICLE

Fast diffusion kurtosis imaging for venous stroke caused by cerebral venous thrombosis

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Abstract: Background: Diffusion kurtosis imaging (DKI) has been found to be more precise than diffusion weighted imaging (DWI) for detecting irreversible infarction in acute ischemic stroke. This study aimed to evaluate whether fast DKI has distinctive advantages in detecting venous stroke caused by cerebral venous thrombosis (CVT). **Methods:** All data from patients diagnosed with venous stroke due to CVT and qualified for mechanical recanalization treatment were collected. Fast DKI and DWI were obtained both before and after revascularization therapy, and lesions were measured. Lesion volumes on T_2 weighted imaging (T_2WI) were followed up at six months. **Results:** A total of 11 patients were recruited. Compared to the contralateral brain, ADC values of the lesions in pre-operation increased significantly (1340.12±235.42 *vs* 919.75±128.98, $P < 0.05$), while MK decreased (0.59±0.11 *vs* 0.81±0.12, $P < 0.05$). And the same changing trend about ADC values (1258.94±185.08 *vs* 949.81±148.52, $P < 0.05$) and MK values (0.64±0.12 *vs* 0.83±0.12, $P < 0.05$) in post-operation. There was no significant difference in the volume of lesions between DKI and DWI during the same examination period (26.97 *vs* 29.28, $P_{\mathrm{pre}} > 0.05$; 13.34 *vs* 13.14, $P_{\mathrm{post}} > 0.05$). However, the lesion volume after revascularization was significantly reduced compared to the first DKI and DWI examinations (26.97 *vs* 13.34, $P < 0.05$), and the same as DWI (29.28 *vs* 13.14, $P < 0.05$). Volume of T_2WI lesions after the 6th month diminished significantly compared with both DKI lesions and DWI lesions before treatment (7.25 *vs* 26.97, $P < 0.05$; 7.25 *vs* 31.19, $P < 0.05$). Fast DKI had a higher signal to noise ratio (SNR) than traditional DKI and DWI. **Conclusion:** The MK of the venous stroke lesions decreased significantly in the subacute stage of CVT, suggesting reversible infarction. Fast DKI has more distinctive superiority in the evaluation of venous stroke. Fast DKI approach may hold great promise for patients in clinical setting because of a higher SNR than DWI. But the sample need to be further expanded because of only 11 patients recruited.

Keywords: diffusion kurtosis imaging, cerebral venous thrombosis, venous stroke

1 Introduction

Cerebral venous thrombosis (CVT) is a relatively rare but potentially fatal neurological condition if overlooked or not diagnosed promptly, owing to its vague nature of its clinical and radiological presentation [1]. MRI with DWI sequence is considered the gold standard for diagnosing cerebral infarction secondary to arterial occlusion. However, in venous infarction caused by CVT, the DWI sequence shows considerable heterogeneity because cytotoxic edema and vasogenic edema may coexist. DWI's ability to detect reversible ischemic lesions in venous infarction is limited. [2].

Diffusion kurtosis imaging (DKI) is an emerging MRI technique that measures the degree of the non-Gaussian water diffusion and is sensitive to microscopic structural changes, and the parameter of mean kurtosis (MK) values could sensitively detection of the infarction lesions regardless the stages of stroke [3–6]. In addition, a study showed that DWI lesions with no change in MK are likely to respond favorably to early reperfusion, while lesions with

abnormalities in MK show poor recovery, which may indicate that DKI is capable of stratifying the heterogeneously injured DWI lesion [7–9]. In addition, previous study reported that the fast DKI scanning needs much shorter time (2 minutes) than traditional DKI. However, it remains unknown whether fast DKI has more advantages than DWI in evaluation of venous stroke caused by CVT. In this study, we aimed to evaluate whether fast DKI has more distinctive superiority in the evaluation of venous stroke, and compare with classical DWI.

2 Materials and methods

2.1 Study design and participants

This study was retrospective designed, and patients were collected in our neurology department from 2020 to 2021. The inclusion criteria including: (1) age ranging from18 to 80 years old; (2) diagnosed as venous stroke secondary to CVT and qualified for mechanical recanalization treatment; (3) written informed consent provided by patients or their relatives. In addition, those patients with venous stroke with CT or MRI showing parenchymal hemorrhage and those who concomitant with contraindication of magnetic resonance examination were excluded.

Each patients recruited was assessed by experienced neurointerventionists, and discussions were conducted to determine whether the patients were qualified for mechanical recanalization treatment. All these patients with clinical symptoms and without contraindications were treated with interventional recanalization in the subacute stage (always from 1 week to 1 month) of CVT. Warfarin was given after surgery to maintain the international normalized ratio ranging from 2 to 3.

2.2 Magnetic resonance imaging

MRI scans including fast DKI and DWI were obtained before and after the revascularization. Diffusion and kurtosis lesions were outlined in by an investigator who was blinded to the experiment. Mean kurtosis (MK) values and apparent diffusion coefficient (ADC) values were recorded in both ipsilateral ischemic and contralateral normal regions. Lesions of T_2 weighted imaging (T_2WI) were followed-up at 6 month.

MRI scans (20 slices, 5mm/slice) were performed on a 3.0 T scanner (Siemens Magnetom Trio Tim) with a 32-channel coil. Gradient field density was 45mT/m. As follows: T_1-weighted images were acquired using spin echo MRI (repetition time/TE = 156 ms/2.55 ms, acquisition matrix = 210 × 256, voxel = 1.1 mm × 0.9 mm × 5.0 mm, shift angle = 50°, duration = 24 seconds). T_2-weighted images were acquired using fast spin echo MRI (repetition time/TE = 4220 ms/84 ms, acquisition matrix = 237 × 320, voxel = 1.0 mm × 0.8 mm × 5.0 mm, shift angle = 160°, duration = 31 seconds). Diffusion-weighted images were obtained from single exciting echo-plannar imaging (EPI) (repetition time/TE = 3000 ms/80 ms, acquisition matrix = 140 × 140, voxel = 1.6 mm × 1.6 mm × 5.0 mm, b = 0, 500, 1000 s/mm^2, duration = 35 seconds). Fast diffusion kurtosis images was performed with parameters as repetition time/TE = 4000 ms/113 ms, acquisition matrix = 128 × 128, voxel = 1.6 mm × 1.6 mm × 5.0 mm, and duration = 2.5 minutes. We also obtained follow-up T_2 MRI 6 months after discharge.

2.3 Imaging analysis and statistics

Mricron.exe and Dcm2niigui.exe were used to record parameters and measure lesions volume. Every parameter acquired was repeated one time and averaged. Lesions mirrored to the contralateral brain acted as reference region of interest. Results were reported as mean±SD.

SPSS19.0 statistical software was used to process data. Description of measurement data was mean±SD or median. Comparison of measurement data was T-test. Nonparametric test used Wilcoxon-test if necessary. All test results were considered significant if p-values were below 0.05.

3 Results

3.1 Demographic characteristics

Baseline characteristics are summarized in Table 1. A total 11 patients (male = 2, female = 9) with a median age of 32.0±11.8 years (ranging from 19 to 52 years) were identified and included in our study. The median time from onset to hospitalization was 14.6±8.5 days

(ranging from 5 to 30 days). Time from onset to the first MRI scanning was 8-30 days, with an average of 18.6±8.0 days. And the time from onset to the second MRI scanning (after surgery) was 10-38 days, with an average of 24.3±8.6 days. Mechanical fragmentation of the related cerebral veins/sinuses were performed. The occluded veins/sinuses got partially or completely recanalization after the interventional treatment with the digital subtraction angiography (DSA) verified. All the patients were stable after the operation without severe complications (parenchyma hemorrhage, subdural hematoma, *etc*.).

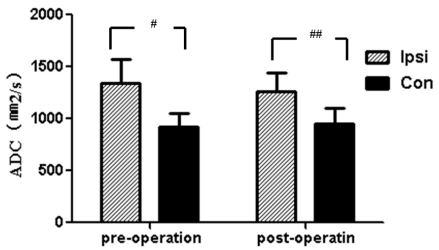
Table 1 Baseline characteristics

No.	Sex	Age (year)	OTH (day)	OTFM (day)	OTSM (day)	Manifestations	Venous Sinuses	Venous Stroke	Possible Risk Factors
1	M	52	13	18	23	somnolence, paralysis	SSS, RTS, RSS	left frontal lobe	Unknown
2	F	19	6	9	10	headache aphasia	Straight sinus LTS, LSS	bilateral thalamus, left basal ganglia region	puberty metrorrhagia
3	F	30	19	20	23	aphasia, paralysis epilepsy	SSS, RTS, RSS	left frontal lobe	puerperium
4	F	46	5	8	16	somnolence paralysis	Straight sinus, Galen vein	bilateral thalamus, left basal ganglia region	hyperthyroidism
5	F	30	30	30	38	paralysis epilepsy	SSS, LTS, RTS, LSS, RSS	left frontal lobe	puerperium
6	F	31	28	30	36	paralysis numbness	SSS, LTS, LSS	right parietal lobe	PNH
7	M	24	14	14	21	epilepsy	SSS, RTS, RSS Straight sinus	left parietal lobe	teratoma
8	F	50	19	25	31	somnolence paralysis	SSS, LTS, RTS, LSS, RSS	left frontal, temporal and parietal lobe	Unknown
9	F	24	9	19	25	epilepsy, tinnitus	SSS, LTS, RTS Straight sinus	bilateral parietal and occipital lobe	puerperium
10	F	22	9	13	21	headache, fever	LTS, LSS	left temporal and occipital lobe	puerperium
11	F	24	9	12	18	paralysis epilepsy	SSS	right frontal and parietal lobe	puerperium

Notes: M: male; F: female; OTH: onset to hospitalization; OTFM: onset to the first MRI scanning; OTSM: onset to the second MRI scanning; SSS: superior sagittal sinus; RSS: right sigmoid sinus; LSS: left sigmoid sinus; RTS: right transverse sinus; LTS: left transverse sinus; PNH: paroxysmal nocturnal hemoglobinuria.

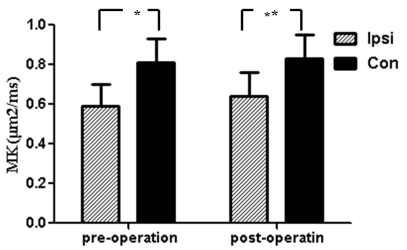
3.2 Comparison of parameters

Figure 1 and 2 show ADC and MK values changed from pre-operation to post-operation respectively in comparison with the contralateral brain mirrored. In both pre-operation and post-operation period, Figure 1 shows ADC of the ipsilateral ischemic regions increased significantly from the contralateral normal regions (1340.12±235.42 *vs* 919.75±128.98, $P < 0.05$; 1258.94±185.08 *vs* 949.81±148.52, $P < 0.05$). While from Figure 2, MK decreased significantly from the contralateral normal regions (0.59±0.11 *vs* 0.81±0.12, $P < 0.05$; 0.64±0.12 *vs* 0.83±0.12, $P < 0.05$). Compared with pre-operation, ADC values decreased and MK values increased in post-operation, but both of them changed insignificantly(1258.94±185.08 *vs* 1340.12±235.42, $P > 0.05$; 0.64±0.12 *vs* 0.59±0.11, $P > 0.05$).



Notes: ADC increased from the contralateral before the operation, # $P < 0.05$; ADC increased from the contralateral after the operation, ## $P < 0.05$.

Figure 1 Ipsilateral ADC values compare with contralateral ADC in different phases



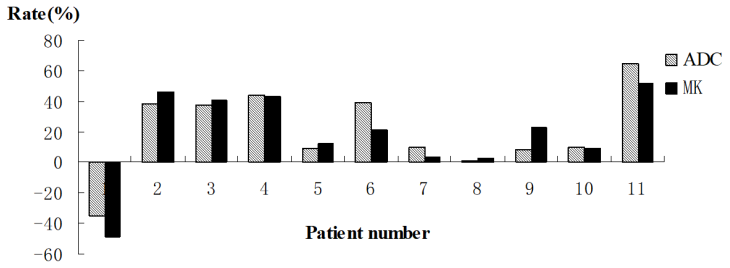
Notes: MK decreased from the contralateral before the operation,* $P < 0.05$; MK decreased from the contralateral after the operation, ** $P < 0.05$.

Figure 2 Ipsilateral MK values compare with contralateral MK in different phases

3.3 Comparison of volume

Volume of DKI lesions showed negligible change from DWI lesions before intervention treatment (26.97 *vs* 29.28, $P > 0.05$). While after the mechanical recanalization therapy, DKI lesions and DWI lesions still manifested little change (13.34 *vs* 13.14, $P > 0.05$). Ten of 11 patients got significantly smaller lesions in post-operation from pre-operation no matter in DKI or DWI scans (26.97 *vs* 13.34, $P < 0.05$; 29.28 *vs* 13.14, $P < 0.05$). Rate of volume change

($(Vol_{pre}\text{-}Vol_{post})/Vol_{pre} \times 100\%$) about pre-operation and post-operation had no significant difference between DWI and DKI scans. (see in Figure 3)



Notes: One female patient got larger volume after interventional operation, but she had no clinical deterioration, and in the 6^{th} month, she got smaller volume than initial MRI scans.

Figure 3 Rate of volume change in different phases of treatment in 11 patients

3.4 Volume at 6-month follow up

Seven of the 11 patients were followed-up in the 6th month after discharge in our department. All of them had no relapsing lesions. Volume of T_2WI lesions minished obviously compared with both DKI lesions and DWI lesions in pre-operation period (7.25 *vs* 26.97, $P < 0.05$; 7.25 *vs* 31.19, $P < 0.05$). Volume of T_2WI lesions disappeared completely in the 6th month in 2 patients. (see in Table 2)

Table 2 Lesion volume at 6-month follow up (mm^3)

No.	Volume of pre-operation		Volume of the 6^{th} month	Rate of volume change	
	ADC map	MK map	T_2WI	ADC%*	MK%#
1	9.40	8.68	1.98	78.94	77.19
2	17.40	18.52	0.00	100.00	100.00
3	31.19	26.97	7.62	75.57	71.75
4	76.95	66.35	31.09	59.60	53.14
5	2.77	3.30	0.00	100.00	100.00
6	54.74	69.27	27.64	49.51	60.10
7	58.04	49.25	7.25	87.51	85.28

Notes: * showed the rate of volume change in DWI and T_2WI lesions; # showed the rate of volume change in DKI and T_2WI lesions.

3.5 SNR of DKI

The study published has suggested that the fast DKI scanning needs just 2 minutes, the same as DWI scanning, but faster than traditional DKI. Fast DKI has a higher SNR than traditional DKI and DWI [10].

4 Discussion

In this study, the recruited 11 patients (M/F = 2/9) had a median age of 32.0±11.8 years (ranging from 19 to 52 years), in accordance with the research published that CVT predominantly affects young adults and it is more common among women than men [11]. It may result from the rare morbidity and delay of outpatient that the participants in our study are all in the subacute but not acute stage of CVT. It is known that CVT always results venous stroke and further aggravates clinical deterioration. Cytotoxic edema and vasogenic edema could exist in venous stroke simultaneously, which is different from arterial ischemic stroke [12]. Venous flow obstruction is thought to result in raised intracranial pressure, decreased cerebral blood flow, and reduced cerebral perfusion pressure, subsequently leading to cytotoxic edema. As a result of venous congestion and disruption of the blood-brain barrier, the net capillary filtration increases, leading to progressive vasogenic edema. The complicated physiopathologic mechanism explains the heterogeneous manifestation on DWI scans. Experimental results suggested that decreased ADC values reflect cellular edema and that increased ADC values correspond to vasogenic edema [13]. ADC values change dynamically during the different stages of CVT. What needs pay attention to is that ADC values may represent vasogenic edema with curability, but also mean the irreversible infarction tissues, especially in the subacute stage of stroke. As previously reported, ADC values increase gradually evolving from subacute to chronic period of arterial ischemic stroke [14]. Increased ADC values only perhaps cannot distinguish reversible ischemic

area from irreversible infarction lesions in venous stroke. There has been no research whether DKI has superiority in screening reversible lesions resulted from venous stroke.

Our study is the first time to discuss the distinction of fast DKI scans on venous stroke and make a comparison with classical DWI. Our study showed that ADC values increase prominently and MK values decrease remarkably from the contralateral normal area in either pre-operation or post-operation period. Conclusions from published papers suggested MK values increase significantly in arterial ischemic stroke in both clinic trials [6, 7, 15] and animal models [2], which mean irreversible infarction. We found the opposite result of MK from previous researches, speculating the reversible ischemic lesions of venous stroke. And we could further speculate the increased ADC of subacute venous stroke represent vasogenic edema. More advantageous than ADC values, MK values have great potential for identifying reversible ischemic lesions in venous stroke, but still need to expand the sample.

Lesions volume on DKI and DWI are not significantly different in the same examination period ($P_{\mathrm{pre}} > 0.05$, $P_{\mathrm{post}} > 0.05$). But lesions after mechanical recanalization treatment get remarkably decreased in both DKI and DWI scans($P_{\mathrm{DKI}} < 0.05$, $P_{\mathrm{DWI}} < 0.05$). In other words, fast DKI lesions also decrease in the subacute phase of CVT, which is different from arterial stroke reported. The volume on T_2WI scans of the followed up in the 6^{th} month gets more smaller ($P < 0.05$), further demonstrating the reversible venous ischemic lesions. All the participants in our study have achieved well clinical outcomes. Decreased MK values and reduced volume both show that the subacute venous stroke may be saved with recanalization therapy. Fast DKI could be important in determining the quality of venous damage, and perhaps patients' outcome, but the sample need to be further expanded. Besides, fast DKI has a higher SNR than traditional DKI and DWI, making which has great application preponderance for clinical schedule [10].

The reasonable explanation for reversible venous stroke is the compensation of venous collateral circulation [16]. Collateral veins may maintain perfusion to the affected brain tissue, thus the tissue involved just be ischemic but not completely infarcted [17]. The damaged brain cells can recover when recanalization obtained. Despite in the subacute stage of CVT, mechanical recanalization treatment may be benefit for patients with venous stroke because of salvageable lesions.

The shortage for this study is a small sample collected because of the low incidence of CVT with venous stroke. Thus makes statistical analysis inefficient. And the sample just comes from our single center and is not fully representative of the CVT patients. Potential bias can not be avoided. Calculation of lesions volume may be not so accurate since the shape of venous stroke varies. Because of the low incidence of CVT and patient delay, we cannot report the ADC and MK in acute venous stroke. But fast DKI scans could exactly provide a guide for therapeutic decision-making and prognosis of CVT patients.

5 Conclusion

MK of the venous stroke lesions decreases significantly in the subacute stage of CVT, suggesting the reversible lesions, which makes up for the deficiency of DWI. Fast DKI approach may hold great promise for patients in clinical setting because it has a higher SNR. And the fast DKI may contribute to clinical interventional therapy and prognosis of subacute stage venous stroke of CVT patients.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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