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ORIGINAL ARTICLE

Diffusion tensor magnetic resonance imaging in assessment of prognostic outcome of stroke patients

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KEYWORDS

MRI;
Diffusion tensor;
Tractography;
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Abstract *Purpose:* The purpose of this study was to assess the utility of diffusion tensor MR imaging as a prognostic imaging technique to detect the clinical outcome in patients presenting with cerebrovascular stroke.

Subjects and methods: The study was conducted on 50 cases presenting with different types of stroke between May 2012 and November 2013. We assessed our patients according to the size of stroke, NIHSS score, degree of reduction of FA and pattern of WM tract affection. Patients presenting with acute ischemic stroke were followed up clinically after 3 months for residual neurological deficits.

Results: We found good association between tractography findings and clinical score at admission as well as the clinical recovery on the follow-up after 3 months. Patients with disruption of white matter tracts had residual deficits on follow-up, whereas patients with displaced and preserved tracts had near complete neurological recovery.

Conclusion: DTI can visualize the changes in the integrity and orientation of the white matter tracts that are affected by cerebrovascular lesions which cannot be detected by conventional MRI. By MR tractography, we can detect the pattern of white matter tract affection that offers a potential tool for correlating the clinical outcome with the imaging findings.

1. Introduction

Stroke is one of the leading causes of death worldwide, especially in the elderly population. As a broad clinical term, it includes patients with arterial ischemic infarcts, intracranial hemorrhage, subarachnoid hemorrhage, and venous infarction (1).

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Recent advances in MR methodologies now enable rapid identification of ischemic tissue in acute stroke. Techniques such as diffusion weighted imaging (DWI) appear to delineate infarcted tissue. Abnormalities demonstrated using MR perfusion imaging potentially identify areas at risk of infarction in the ischemic penumbra. The challenges in imaging of very early stroke are centered on the identification of potentially salvageable tissue and the assessment of whether there is a major vascular occlusion or not, the aim being to give appropriate targeted therapy to identifiable subtypes of stroke. A less well addressed problem relates to the use of imaging to provide prognostic information regarding clinical outcome (2).

Conventional MR imaging cannot provide reliable information about the integrity of white matter tracts, thereby limiting the ability to predict clinical outcome (1).

Diffusion imaging is an MRI imaging technique that is sensitized to the Brownian motion of water molecules in biological tissues. White matter in the brain is anatomically present in different directions, so diffusion in the brain is not uniform but anisotropic, along the direction of the various fiber tracts. Therefore, the measure of diffusion cannot be represented as a single quantity but is modeled by estimation of a diffusion tensor (D), which is the measurement of water diffusion in different directions (3).

DTT is promising for stroke mapping to predict motor outcome. Diffusion tensor imaging and MR tractography techniques can be used to evaluate the structural degeneration of white matter tracts following stroke (1,4).

The ability to identify white matter tract disruption in acute stroke may be a useful index of stroke severity and may allow insight into likely recovery and long-term disability (2).

2. Subjects and methods

2.1. Patients

This study was conducted on 50 patients (30 males and 20 females) between May 2012 and November 2013. Age range between 24 and 80 years referred from the neurology department to the radiology department. Written consents were obtained from all patients. Patients presented with stroke including 48 patient with ischemic stroke (24 acute nonhemorrhagic, 6 acute with hemorrhagic conversion and 18 chronic stroke) and 2 primary intracerebral hemorrhage.

The time of imaging varied from less than one week to more than eight weeks after the onset of acute symptoms.

Clinical neurological deficits were evaluated by a neurology specialist using the National Institutes of Health Stroke Scale (NIHSS) on admission.

The patients presenting with acute ischemic stroke (hemorrhagic or nonhemorrhagic) were followed up clinically after 3 months for residual neurological deficits.

The interval changes of the NIHSS scores were assessed and neurological improvement was defined as a decrease of points in the NIHSS score

2.2. MR examination

MRI was done without prior preparation or anesthesia and after the exclusion of MRI contraindications as cardiac pacemaker, claustrophobia, etc.

2.3. Technique

2.3.1. Acquisition

Technique was performed using a standard 1.5 Tesla unit (Intera and Achieva, Philips).

- A standard head coil was used.
- The sequences obtained were axial T1 W, T2 W, FLAIR, DW and Diffusion tensor.
- Diffusion tensor consisted of the following:
  - A single shot, spin-echo echoplanar sequence in 12 encoding directions.
  - A diffusion weighting factor of 800 s/ mm^2.
  - TR 8000 ms.
  - TE 67 ms.
  - Flip 90°.
  - Matrix 112 × 110.
  - FOV 210 × 236 mm.
  - Number of excitations: 2.
  - Slice thickness: 2.0/00.

- All the images were transferred to the workstation (Philips Extended MR Workspace, 2.6.3.5, Netherlands) for postprocessing.

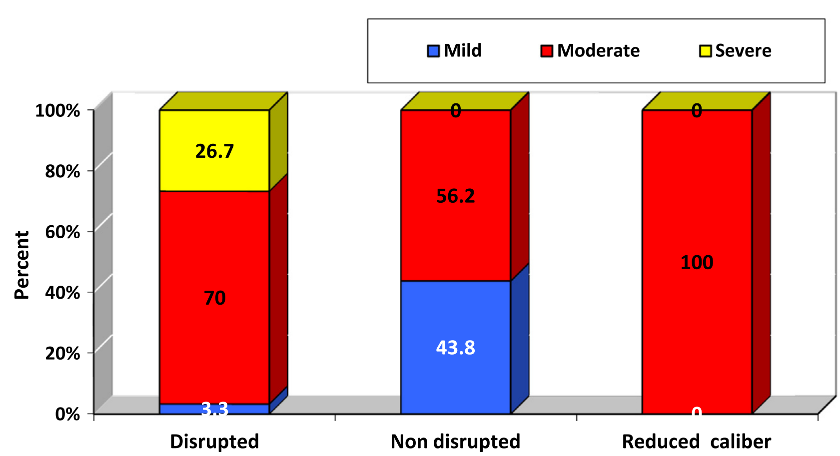

Fig. 1 Association between pattern of WM tracts involvement detected by FT and NIHSS on admission in the studied group.

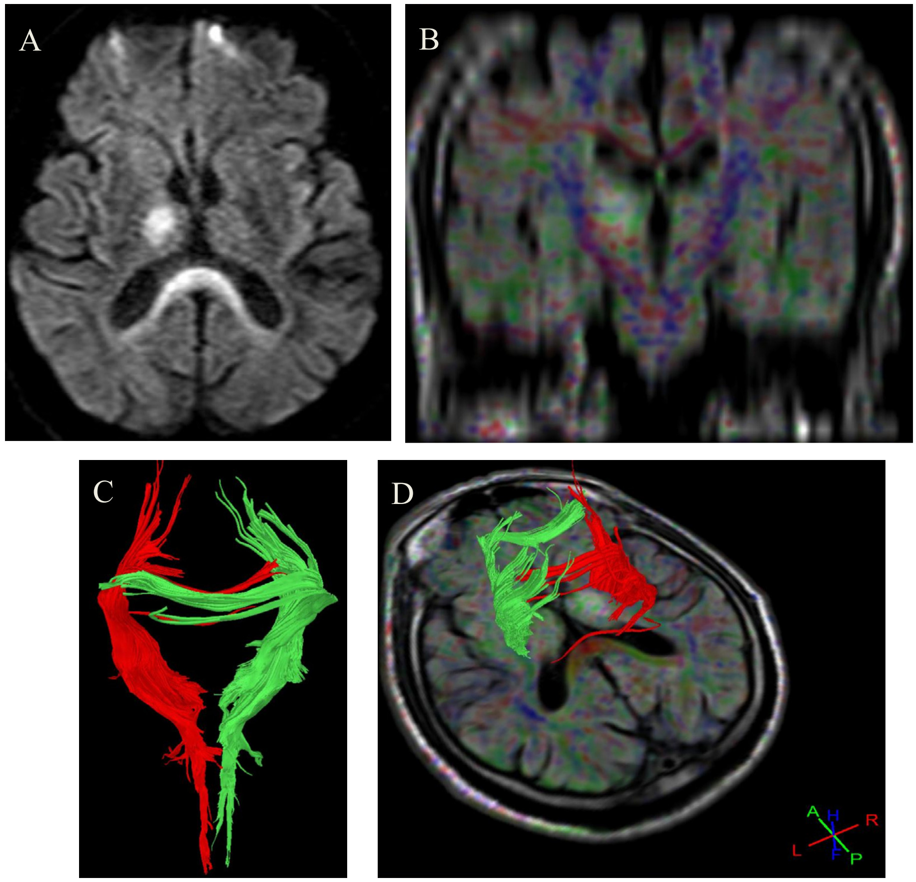

Fig. 2 (A) Axial diffusion WIs (b1000) in a 45 years old male presented with left paresthesia shows right thalamic area of restricted diffusion (acute infarct). (B) Coronal FA color coded map overlaid over coronal FLAIR image. (C) 3D fiber tractography of the CST. (D) Axial FA color coded map overlaid over axial FLAIR image with 3D tractography of the CST showing preserved fibers of the right CST. Patient shows minimal residual sensory neurological deficit (NIHSS after 3 months was 2).

2.3.2. Processing

Following are the maps obtained:

(1) FA maps.
(2) Directionally-encoded color FA maps.
(3) 3D fiber tractography.

- The direction and anatomy of the tracts are seen in the directionally encoded FA maps, where a specific color is assigned to tracts running in the three orthogonal planes: red is for right to left tracts, green for antero-posterior tracts, and blue for cranio-caudal tracts.
- The FA values were measured at the region of abnormality and were compared with the normal values on the unaffected contralateral side.
- MR tractography of the white matter tracts was performed based on known anatomy. Regions of interest (ROIs) were drawn as seeds in the uninvolved portions of the white matter tracts (multi-ROI technique), and the software algorithm tracked the white matter tracts that passed through these ROIs.

2.3.3. Interpretation

Color-coded DTI maps were analyzed, followed by tractography of individual tracts. DTI data and MR tractography of the involved white matter tracts were compared with the corresponding tracts of the contralateral normal hemisphere. The tracts were visually inspected for changes in size and orientation, and compared to those in the contralateral hemisphere. The tracts were characterized as either displaced or disrupted, based on the system proposed by Witwer et al. (5). They were considered displaced if they maintained normal anisotropy relative to the corresponding tract in the contralateral hemisphere but had abnormal location or orientation; and disrupted if anisotropy was markedly reduced such that the tract could not be identified on the DTI based maps and/or by the failure of the fiber tracking algorithm.

Some patients showed decrease in the size of the CST, but it was intact throughout its extent. This is attributed to wallerian degeneration.

2.4. We categorized the patients included in this study according to the following:

- The FA value:
  - Mild (0.4)
  - Moderate (0.2–0.3)
  - Severe (0.1)

- Tractography:
  - Nondisrupted ‘‘preserved’’ if there are no tracts affected by the lesion (Fig. 2).

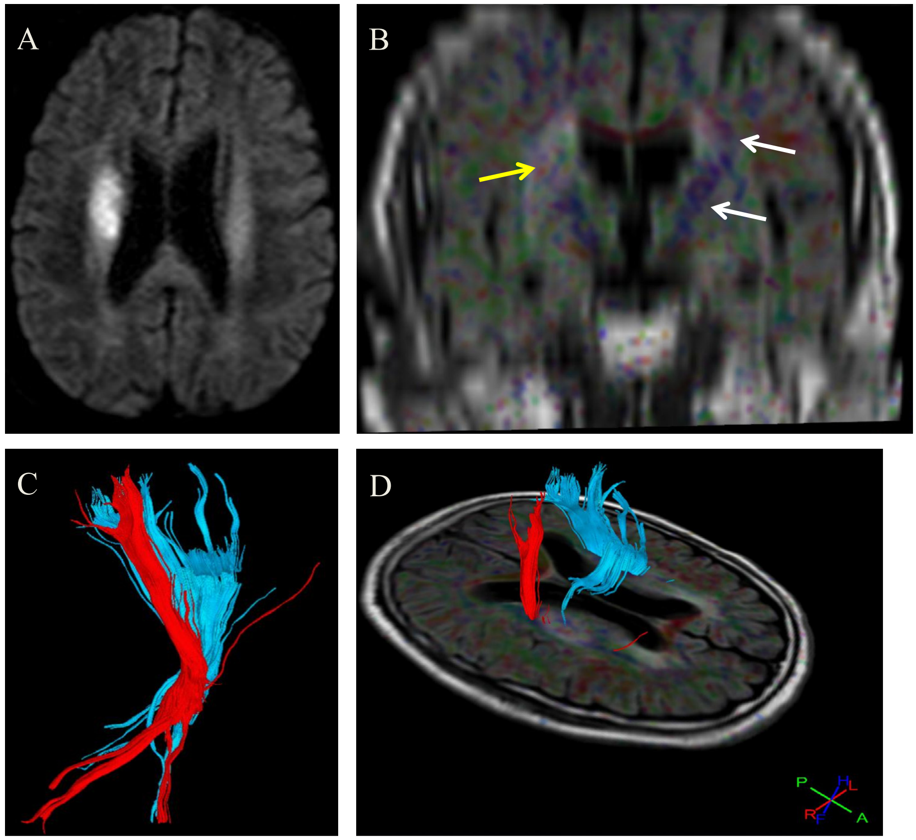

Fig. 3 (A) Axial diffusion WIs (b1000) in a 64 years old male presented with left hemiplegia shows right corona radiata area of restricted diffusion (acute infarct). (B) Coronal FA color coded map overlaid over coronal FLAIR image. (C) 3D fiber tractography of the CST. (D) Axial FA color coded map overlaid over axial FLAIR image with 3D tractography of the CST showing disrupted anterior fibers of the corona radiata (yellow arrow) compared to the left side (white arrow). Patient showed mild clinical improvement with residual neurological deficit (NIHSS after 3 months was 4).

  - Disrupted if at least one tract is disrupted (Figs. 3 and 4).
  - Nondisrupted "displaced" if one tract is displaced while other tracts related to the lesion are not affected (Fig. 4).
  - Reduced caliber if at least one tract shows reduced caliber with no other tracts show disruption (Fig. 5)

- Size of infarction:
  - Small (< 3 cm)
  - Medium sized (3–8 cm)
  - Large (> 8 cm)

- Clinical NIHSS score:
  - Mild (1–4)
  - Moderate (5–10)
  - Severe (> 10)

2.5. Statistical analysis

- Results are expressed as mean ± standard deviation or number (%).
- Association between FA site of lesion, tractography and different studied parameters was performed using Chi square test.
- SPSS computer program (version 16 windows) was used for data analysis.
- *P* value less or equal to 0.05 was considered significant and less than 0.01 was considered highly significant.

3. Results

- The association between pattern of WM tracts involvement detected by FT and NIHSS on admission was studied (Table 1, Fig. 1).
  - Among the 30 patients in the disrupted group, 1 patient (3.3%) was belonging to the mild NIHSS group, 21 patients (70%) were belonging to the moderate group and 8 patients (26.7%) were belonging to the severe group.
  - In the nondisrupted group 7 patients (43.8%) were belonging to the mild NIHSS group while 9 patients (56.2%) were belonging to the moderate group.
  - All the 4 patients in the reduced caliber group were belonging to the moderate NIHSS group.
  - There was a statistical significant association between them ($p = 0.001$).

- The association between degree of FA reduction at the site of the lesion and the NIHSS on admission was studied.
  - Among the 37 patients in the moderate FA group, 7 patients (18.9%) were belonging to the mild NIHSS group, 24 patients (64.9%) were belonging to the moderate group and 6 patients (16.2%) were belonging to the severe group.

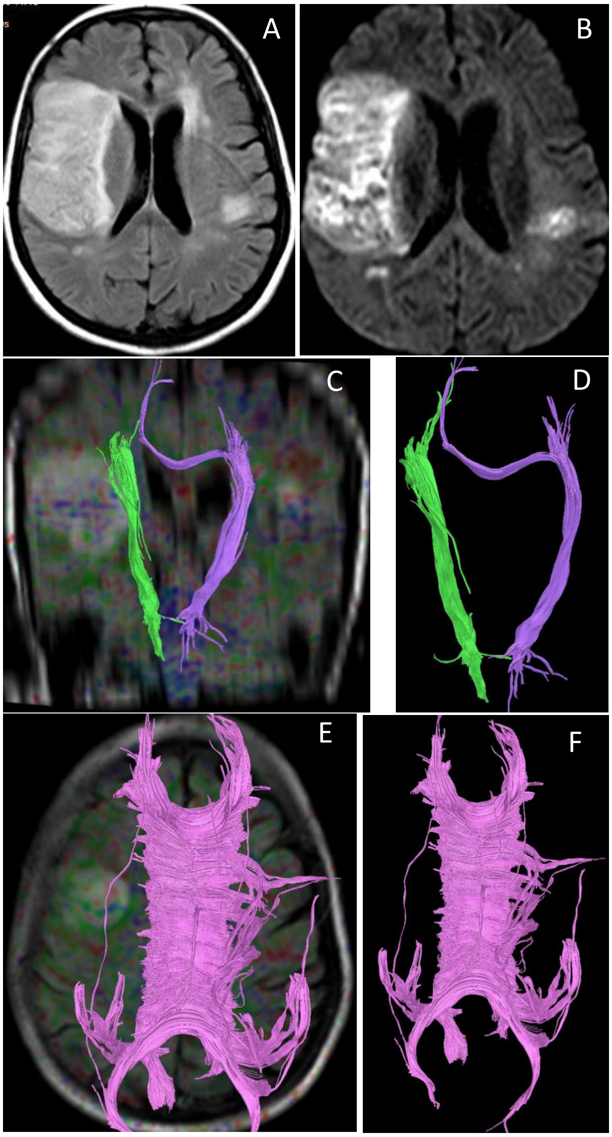

Fig. 4 (A) Axial FLAIR WIs in a female patient 60 years old presented with left hemiplegia show cortical and subcortical area of high signal at the right parietal region measuring about 8.5×4 cm in diameters. (B) Axial diffusion WIs (b1000) show restricted diffusion of the lesion. Note the smaller left parietal acute infraction. (C) Coronal FA color coded map overlaid over coronal FLAIR image with fiber tractography of the CST. (D) 3D fiber tractography of the CST. The right CST (green) appears displaced medially by the lesion yet it appears preserved. (E) Axial FA color coded map overlaid over axial FLAIR image with fiber tractography of the CC. (F) 3D fiber tractography of the CC. The right tapetum and right fibers of the body of the corpus callosum appear disrupted.

- In the severe FA group 1 patient (9.1%) was in the mild NIHSS group, 9 patients (81.8%) were in the moderate group and 1 patient (9.1%) was in the severe group.
- On the other hand, among the two patients with mild FA at the site of the lesion, 1 patient (50%) was in the moderate NIHSS group and the other patient (50%) was in the severe group.
- There was no statistical significant association between them ($p = 0.545$).

- The association between degree of FA reduction at the site of the lesion and the size of the lesion was studied.
  - Among the 37 patients in the moderate group, 20 patients (54.1%) had small lesions, 13 patients (35.1%) had medium sized lesions and 4 patients (10.8%) had large lesions. While in the severe group 3 patients (27.3%) had small lesions, 5 patients (45.5%) had medium sized lesions and 3 patients (27.3%) had large lesions. On the other hand, among the two patients with mild FA at the site of the lesion, 1 patient (50%) had small lesion and one patient (50%) had medium sized lesion.
  - There was no statistical significant association between them ($p = 0.475$).

- The association between pattern of WM tracts involvement detected by FT and the size of the lesion was studied.
  - Among the 30 patients in the disrupted group, 8 patients (26.7%) had small lesions, 15 patients (50%) had medium sized lesions and 7 patients (23.3%) had large lesions.
  - In the nondisrupted group 12 patients (75%) had small lesions, and 4 patients (25%) had medium sized lesions.
  - All the 4 patients in the reduced caliber group had small sized lesions.
  - There was a statistical significant association between them ($p = 0.004$).

- The association between pattern of WM tracts involvement detected by FT and NIHSS on admission was studied.
  - Among the 30 patients in the disrupted group, 1 patient (3.3%) was belonging to the mild NIHSS group, 21 patients (70%) were belonging to the moderate group and 8 patients (26.7%) were belonging to the severe group.
  - In the nondisrupted group 7 patients (43.8%) were belonging to the mild NIHSS group while 9 patients (56.2%) were belonging to the moderate group.
  - All the 4 patients in the reduced caliber group were belonging to the moderate NIHSS group.
  - There was a statistical significant association between them ($p = 0.001$).

- The Mean FA of the brain parenchyma of the contralateral side of the lesion was calculated and correlated to the degree of FA reduction at the site of the lesion The lowest value on the contralateral side was found in the severe FA group at the site of the lesion.
- Association between FA reduction at the site of the lesion and the NIHSS after 3 months in the 30 patients presenting with acute ischemic stroke was studied. No statistical significant association was detected ($p = 0.474$).
- Association between pattern of WM tracts involvement detected by FT and the NIHSS after 3 months in the 30 patients presenting with acute ischemic stroke was studied. Moderate NIHSS measured after 3 months was highly present in 15 (83.3%) out of 18 disrupted patients when compared with both nondisrupted [0(0%)] and reduced caliber [2 (66.7%)] which were statistically significant ($p < 0.001$).

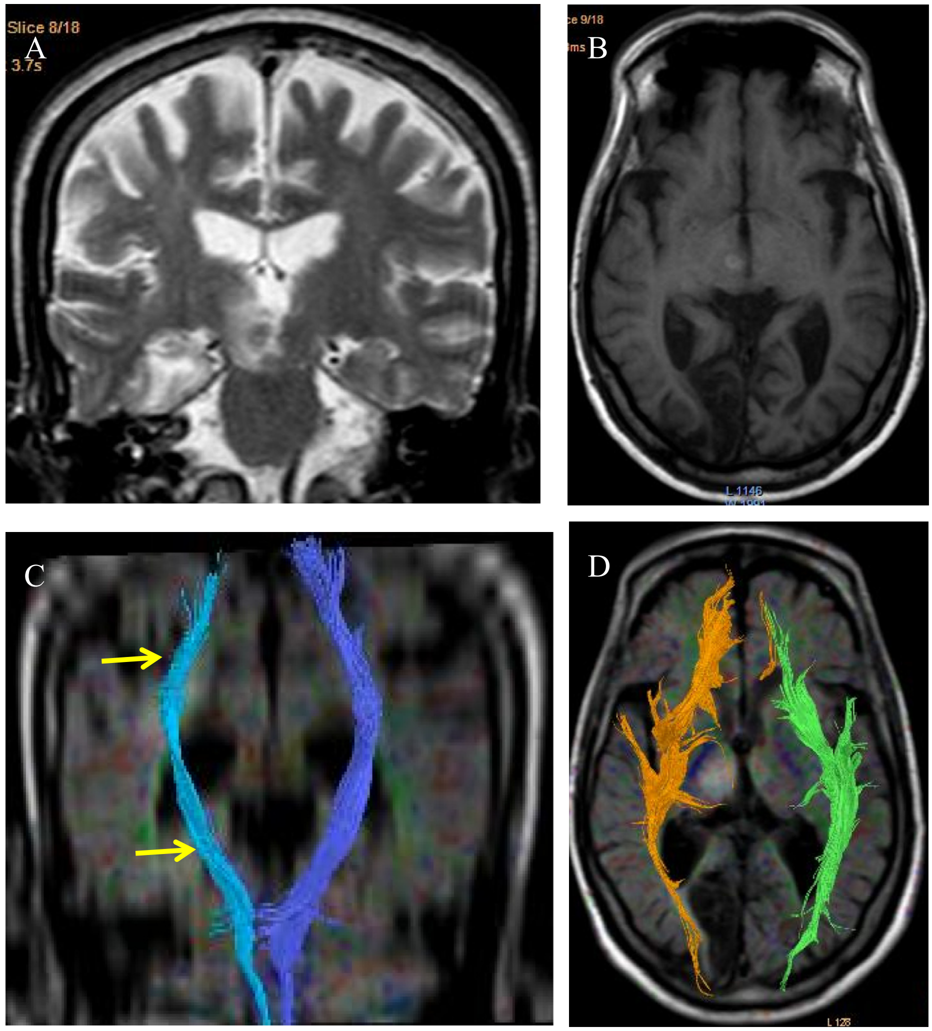

Fig. 5 67 years old female patient with history of old stroke presented with left sided weakness. (A) Coronal T2 WIs shows small right thalamic and right cerebral peduncle infarction measuring about 1.5×1.2 cm in diameters. (B) Axial T1 WIs shows small hemorrhagic component of the right thalamus and right occipital encephalomalacia. (C) Coronal FA color coded map overlaid over coronal FLAIR image with fiber tractography of the CSTs showing reduced caliber of the right CST throughout its course (arrows). (D) Axial FA color coded map overlaid over axial FLAIR image with fiber tractography of the IFO fasciculi showing reduced caliber of the posterior part of the right IFOF (orange).

Table 1 Association between pattern of WM tracts involvement detected by FT and NIHSS on admission in the studied group.

		Tractography			*P* value
		Disrupted (n = 30)	Nondisrupted (n = 16)	Reduced caliber (n = 4)	
NIHSS	Mild	1 (3.3%)	7 (43.8%)	0 (%)	0.001**
	Moderate	21 (70%)	9 (56.2%)	4 (100%)	
	Severe	8 (26.7%)	0 (0%)	0 (%)	

Data are expressed as number (%).
** $p < 0.01$ = highly significant.

4. Discussion

The recovery from stroke early in the disease has been implicated to the resolution of tissue edema and mass effect associated with infarction and hemorrhage. However, for long-term recovery, relative preservation of the integrity and anisotropy of the white matter tracts (corticospinal tract particularly) plays an important role and indicates a better clinical outcome. Conventional imaging however does not give data about the microstructural organization of the white matter fiber tracts, which can be obtained from DTI and MR tractography (1).

Our study was performed to assess the utility of MR diffusion tensor imaging as a prognostic imaging technique to detect the clinical outcome in patients presenting with cerebrovascular stroke.

We found good association between tractography findings and clinical score at admission as well as the patient's clinical recovery on the follow-up after 3 months. All the patients with disruption of white matter tracts had residual deficits on clinical follow-up, whereas the patients with displaced and preserved tracts had near complete neurological recovery. This indicates that fiber tractography is well correlated with the clinical presentation of the stroke patients i.e. the more the severe the clinical presentation the more the affection of the WM tracts detected by tractography. And according to Kwon et al., 2011 (6) the predictability of DTI for motor outcome is better when done 15–28 days after onset. This also indicates that fiber tractography is well correlated with the clinical outcome of the patients i.e. the patients with severe WM affection will have unfavorable clinical outcome.

Lai et al. (7) examined 28 stroke patients in the acute phase or early subacute phase with a marked motor deficit. With regard to the CST, they divided patients into three clinical subgroups: Group 1 (intact type), Group 2 (partial involvement type) and Group 3 (whole involvement type). Subsequently, the severity of the motor deficit of each patient was determined according to the NIHSS scores at the acute/early subacute phase. NIHSS scores of Group 1 were significantly lower than those of Group 2 at the acute phase or early subacute phase and those of Group 2 were significantly lower than those of Group 3. They also found that at outcome, NIHSS scores of Group 1 were significantly lower than those of Group 2, and scores of Group 2 were significantly lower than those of Group 3. At the same time, the NIHSS scores of each group gradually decreased from acute phase to outcome.

Our results also agreed with the study done by Parmar et al., 2006 (1) who studied 11 cases with stroke and diffusion tensor imaging data were acquired. They found a good correlation between tractography findings and patient's clinical recovery. All the patients with disruption of white matter tracts had residual deficits on clinical follow-up, whereas the patients with displaced tracts had near complete neurological recovery. The patient with wallerian degeneration (corresponding to the reduced caliber group in our study) also continued to show residual motor deficits.

We also found significant statistical association between the pattern of WM tracts involvement detected by FT and the size of the lesion and this may indicate that large lesions are more associated with tract disruption.

We did not find significant association between the FA at the site of the infarction and the clinical score at admission or the clinical outcome after 3 months and we did not find significant statistical association between the size and the degree of FA reduction.

We calculated the mean FA of the brain parenchyma of the contralateral side of the stroke and correlated it to the FA reduction at the site of the lesion. The lowest value on the contralateral side was found in the severe FA reduction group at the site of the lesion. This may indicate that the brain parenchyma of the patients in the severe group is more vulnerable to be severely affected after stroke and shows lower FA values.

5. Conclusion

DTI can visualize the changes in the integrity and orientation of the white matter tracts that are affected by cerebrovascular lesions which cannot be detected by conventional MRI. By MR tractography, we can detect the pattern of white matter tract affection that offers a potential tool for correlating the clinical outcome with the imaging findings.

Conflict of interest

The authors declared that there is no conflict of interest.

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