

Diffusional kurtosis imaging in evaluation of microstructural changes of spinal cord in cervical spondylotic myelopathy feasibility study

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Abstract

To explore the value of diffusion kurtosis imaging in the changes of spinal cord microstructures in patients with early cervical spondylotic myelopathy.

Twenty nine patients with cervical myelopathy were selected in this study. All images were acquired on a 3.0 T MR scanner (Skyra, Siemens Medical Systems, Germany). The imaging parameters for diffusion kurtosis imaging were as follows: repetition time/echo time, 3000/91 ms; averages, 2; slice thickness/gap, 3/0.3 mm; number of slices, 17; field of view, 230 × 230 mm; Voxel size, 0.4 × 0.4 × 3.0 mm; 3 *b*-values (0, 1000, and 2000 s/mm²) with diffusion encoding in 20 directions for each *b*-value. Values for fractional anisotropy, mean diffusivity, and mean diffusional kurtosis (MK) were calculated and compared between unaffected and affected spinal cords.

In all patients MK was significantly lower in normal appearing spinal cords adjacent to the affected cervical spinal cords than in normal cervical spinal cords (0.862 ± 0.051 vs 0.976 ± 0.0924 , $P < .0001$), but the difference of fractional anisotropy and apparent diffusion coefficient was no significant ($P > .05$). The affected cervical spinal cords had lower MK (0.716 ± 0.0753), FA and higher apparent diffusion coefficient than normal cervical spinal cords ($P < .001$).

MK values in the cervical spinal cord may reflect microstructural changes of spinal cord damage in cervical myelopathy, and it could potentially provide more information that obtained with conventional diffusion metrics.

Abbreviations: ACPC = affected cervical spinal cord, DKI = diffusional kurtosis imaging, MK = mean kurtosis, NASC = normal appearing spinal cords adjacent to the affected cervical spinal cord, NCSC = normal cervical spinal cord.

Keywords: cervical spondylotic myelopathy, diffusional imaging, mean kurtosis

1. Introduction

Cervical spondylotic myelopathy is a common degenerative disease that causes several types of motor and sensory

dysfunction. This disease is frequently accompanied with cervical spinal stenosis and cord myelopathy resulted by disc herniation, osteophyte formation, and ossification of the posterior longitudinal ligament. Conventional magnetic resonance imaging is widely used to evaluate morphological changes in cervical spondylotic myelopathy. However, there is a weak correlation between MR Imaging findings and the severity of the illness.

Diffusion kurtosis imaging (DKI) is the minimal extension of Diffusion tensor imaging (DTI) with a genuine diffusion technique accounting for diffusional non-Gaussianity. It could better describe the complicated diffusion behavior in vivo tissues and provide the quantification of non-Gaussian diffusion and reveal more microstructure information^[2-4] Mean kurtosis, a DKI-derived metric, is represented as a new parameter in addition to the diffusion coefficient^[5] that complements MD (mean diffusivity) and FA (fractional anisotropy) values.^[1] Compared with conventional diffusion DTI, DKI can more accurately reflect the in vivo pathological changes of tissue microstructure.^[6,7] Decreased FA values only means degeneration of the white matter in the brain and spinal cord- axonal damage.^[8] However, Graham et al. think microcirculatory disturbance plays an important role in the damage of compressed spinal cord.^[9] The mean diffusion kurtosis (MK) value may be a highly sensitive indicator for assessing changes in the microstructure of spinal cord compression in patients with early cervical spondylotic myelopathy.^[10] The purpose of this study is to investigate microstructural changes in the spinal cord of patients with cervical spondylotic myelopathy by using DKI.

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In this study, MK, FA, and MD values of 3 cervical pulp segments of each patient were measured and then compared with each of the 2 groups (affected cervical spinal cords: T2-weighted imaging (T2WI) shows high signal in the spinal cord; normal appearing spinal cords adjacent to the affected cervical spinal cords: near affected cervical cords and T2WI shows no abnormal signal in the spinal cords; normal cervical spinal cords). In the present study, we aim to determine the feasibility of MK, FA, and MD for evaluation of microstructural changes of spinal cord in cervical spondylotic myelopathy. The utility of the 3 parameters was also examined.

2. Methods

2.1. Study subjects

Twenty-nine patients with cervical spondylotic myelopathy were selected in this study (11 males and 18 females; age range: 45–87 years old; mean age: 61.9 years old). All patients had a series of signs and symptoms, including Neck and Shoulder pain, Neck stiffness, Muscle weakness, Numbness, and difficulty in walking, and so on. Pain is one of the main symptoms prompting a visit to a physician in all patients. The duration of symptoms varies from 3 months to 10 years. All patients presenting with symptomatic spondylotic disease were evaluated by neurosurgeon or neurologist.

Inclusion criteria were as follows:

- (1) patients with symptoms and signs of purely cervical spondylotic myelopathy examined by a neurosurgeon or neurologist;
- (2) Patients with single-level cervical compression;
- (3) patients without any previous spine surgery, history of cervical trauma, and history of stroke and other neurological disease or any radiation and chemotherapy before magnetic resonance imaging examination.

The study was approved by the ethics committee of Shandong Provincial Hospital Group, Shandong University and letters of consent were obtained from all the patients.

2.2. Image acquisition

All images were acquired on a 3.0 T MR scanner (Skyra, Siemens Medical Systems, Germany). Before DKI, conventional spine-choT1- and T2-weighted sagittal and axial images were obtained. Imaging parameters for sagittal images were as follows: repetition time(TR)/echo time (TE), 4000/133 ms for T2WI and 550/9 ms for T1-weighted imaging; averages 2 for T1-weighted imaging T2WI; section thickness/gap, 3/0.3mm; number of slices, 17 sections; field of view, 230 × 230 mm; Voxel size, 0.4 × 0.4 × 3.0 mm. Imaging parameters for axial images were as follows: TR/TE 2770/112 ms; averages 2; section thickness/gap, 4/0.4 mm; field of view, 200 mm; Voxel size, 0.3 × 0.3 × 4.0 mm. The imaging parameters for DKI were as follows: TR/TE, 3000/91ms; averages, 2; slice thickness/gap, 3/0.3mm; number of slices, 17; field of view, 230 × 230 mm; Voxel size, 0.4 × 0.4 × 3.0 mm; 3 *b*-values (0, 1000, and 2000 s/mm²) with diffusion encoding in 20 directions for each *b*-value, and acquisition time 11 minutes 39 seconds. Values for FA, apparent diffusion coefficient (ADC), and MK were calculated and compared between the affected cervical spinal cords, normal appearing spinal cords adjacent to the affected cervical spinal cords and normal cervical spinal cords.

2.3. Image interpretation

Data of DKI was analyzed by using in-house software (Diffusion and Kurtosis Estimator) in Matlab, Version Release 2012a /7.14 (MathWorks, Natick, MA) to MK, FA, MD maps. A standardized Region of interest (ROI) size about 20 voxels was drawn in the affected cervical spinal cords, normal appearing spinal cords adjacent to the affected cervical spinal cords and normal cervical spinal cords on the T2WI image, then, the ROI was automatically transferred onto the corresponding MK, MD, and FA map, and mean values of MK, MD, and FA were evaluated. All images were evaluated by 2 experienced radiologists with double-blind method (15 and 20 years of experience in radiology).

2.4. Statistical analysis

Statistical analysis was performed with the Statistical Package for SPSS 22.0. Values of MK, FA, and MD were presented in a form of mean ± standard deviation. The cut-off values of MK, MD, and FA of affected cervical spinal cords, normal appearing spinal cords adjacent to the affected cervical spinal cords and normal cervical spinal cords were obtained with receiver-operating characteristic curve analysis; For testing the consistency of MK, MD, and FA, each of the raw data was compared with the cut-off values. Then, the results of Consistency Checking were compared between MK, MD, and FA by using Calibrate the Chi-square test for affected cervical spinal cords, normal appearing spinal cords adjacent to the affected cervical spinal cords. $P < .05$ was considered to have statistical significant difference and $P < .017$ was considered to have statistical significant difference by using Calibrate the Chi-square test.

3. Results

3.1. Value of MK, FA, and MD in normal appearing spinal cords adjacent to the affected cervical spinal cords, normal cervical spinal cords, and affected cervical spinal cords

The diffusion kurtosis metric values MK, FA, and MD in normal appearing spinal cords adjacent to the affected cervical spinal cords, normal cervical spinal cords and affected cervical spinal cords are shown in Table 1, Figures 1 and 2. Mean MK value was significantly lower in normal appearing spinal cords adjacent to the affected cervical spinal cords than that in normal cervical spinal cords ($P < .0001$), but the difference of FA and ADC was no significant ($P > .05$)

Table 1

MK, FA, and MD values in affected cervical spinal cords, normal appearing spinal cords near affected cervical spinal cords and normal appearing spinal cords in patients with Cervical spondylotic myelopathy.

	MK	FA	MD (10 ⁻³ mm ² /s)	n
ACPC	0.7158 ± 0.07534	0.3885 ± 0.1199	1.5467 ± 0.1548	29
NASCN	0.8617 ± 0.0506	0.5156 ± 0.1031	1.2720 ± 0.2522	29
NCSC	0.9762 ± 0.0924	0.5587 ± 0.06969	1.2531 ± 0.06573	29

ACPC = affected cervical spinal cords, FA = fractional anisotropy, MK = mean kurtosis, MD = mean diffusivity, NASCN = normal appearing spinal cord near affected cervical spinal cords, NCSC = normal cervical spinal cords.

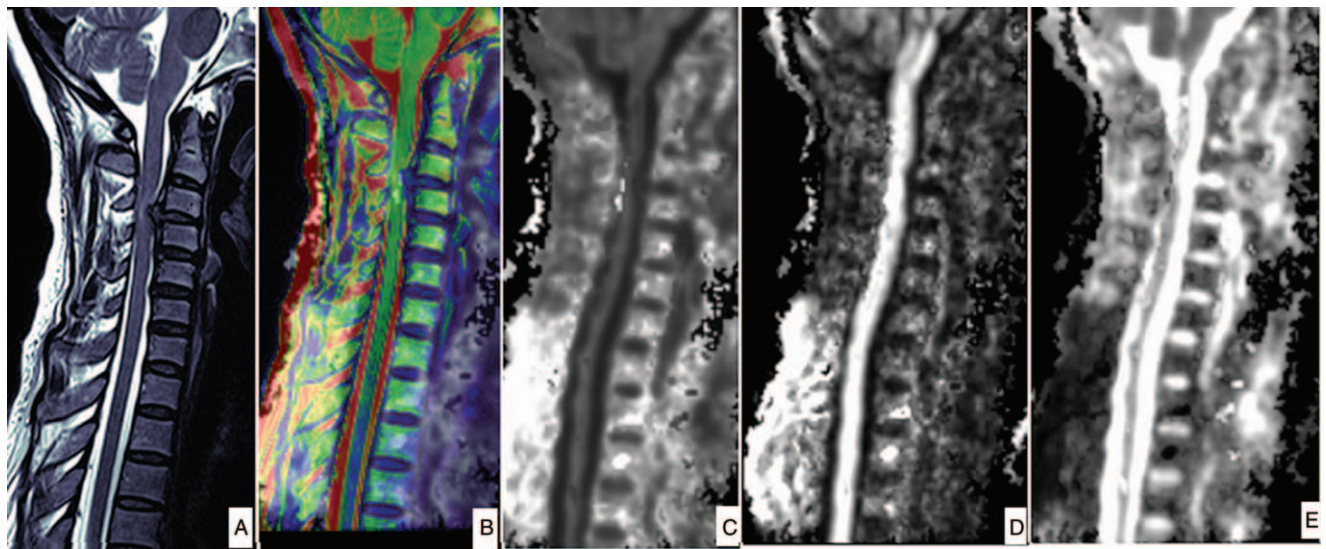


Figure 1. (A) Sagittal T2WI image of patient with cervical spondylotic myelopathy. T2WI shows affected cervical spinal cord (C3/4 disc level) disc herniation, spinal stenosis, compression, deformation, and edema of the corresponding segment of the spinal cord. There is no change in the morphology or signal of the cervical spinal cord in normal appearing spinal cord (C4/5 disc level) adjacent to the affected cervical spinal cord and normal cervical spinal cord (C5/6 disc level). (B) MK map and T2WI pseudo-color fusion map shows that affected cervical spinal cord is compressed and signal change. The morphology and signal of normal appearing spinal cord adjacent to the affected cervical spinal cords is normal; (C–E) MK, FA, and MD map shows MK, FA, and MD value of affected cervical spinal cord, normal appearing spinal cord adjacent to the affected cervical spinal cord, normal cervical spinal cords are 0.6538, 0.2502, 1.5528 and 0.8635, 0.3723, 1.4726, 1.019, 0.5595 and 1.4936, respectively. FA = fractional anisotropy, MD = mean diffusivity, MK = mean kurtosis.

3.2. The consistency and comparison of MK, MD, and FA between normal appearing spinal cords adjacent to the affected cervical spinal cords, normal cervical spinal cords, and affected cervical spinal cords

In order to assess the value of MK values in evaluation of Microstructural Changes of Spinal Cord in Cervical spondylotic myelopathy, Consistency Checking was performed, and the cut-off value was calculated by using receiver operating characteristic analysis. Then, Calibrate the Chi-square test was used between MK, MD, and FA for showing the accuracy of the 3 values.

MK values had a high concordance in normal appearing spinal cords adjacent to the affected cervical spinal cords and affected cervical spinal cords compared with the cut-off value (Table 2). There was significant difference in mean MK values than MD and FA values in normal appearing spinal cords adjacent to the

affected cervical spinal cords ($P < .0001$ and $P = .016$) by using Calibrate the Chi-square test (Fig. 2).

4. Discussion

In this study, pairwise comparison was carried out for affected cervical spinal cords, normal appearing spinal cords adjacent to the affected cervical spinal cords and normal appearing spinal cords in patients with Cervical spondylotic myelopathy by utilizing the DKI technique and Calibrate the Chi-square test. MK, FA, and ADC values change significantly showing obvious statistical difference between affected cervical spinal cords and normal cervical spinal cords. It also happens between affected cervical spinal cords and normal appearing spinal cord adjacent to the affected cervical spinal cords. However only MK values shows significant changes between normal appearing spinal cords adjacent to affected cervical spinal cords and normal cervical spinal cords. There was significant difference found between mean MK values and MD\FA values in normal appearing spinal cord adjacent to the affected cervical spinal cords ($P < .0001$ and $P = .016$) by using Calibrate the Chi-square test. This shows that extensive cervical spinal cord damage not only can cause damage to the adjacent cords but also cause potential damage to normal appearing normal-appearing tissue over time. MK values can reflect spinal damage when T2WI appearing normal in early stage. FA and MD values could not reflect abnormal. So MK is a more sensitive index compared to FA and MD values in reflecting changes in microstructure. And this is consistent with previous DKI studies in Multiple Sclerosis.^[11] DKI was regarded as very valuable for measuring histological properties of tissues as per researches.

Traditional diffusion (DWI and DTI) model assumes that the displacement probability function of diffusing water molecules follows the Gaussian distribution.^[12,13] In fact, water diffusion

Table 2
Variables of Calibrate the chi-square test of MK, FA, and MD in affected cervical spinal cords, normal appearing spinal cords near affected cervical spinal cords and normal appearing spinal cords in patients with cervical spondylotic myelopathy.

	MK vs MD	MK vs FA	FA vs MD	n
ACPC Pearson	7.733 ^a	6.444 ^α	0.083 ^a	58
P	0.005	0.011	0.773	
NASCN Pearson	13.533 ^a	5.836 ^a	1.866 ^a	58
P	<0.001	0.016	0.172	
NCSC Pearson	1.933 ^a	2.805 ^a	0.090 ^a	58
P	0.164	0.094	0.764	

ACPC=affected cervical spinal cords, NASCN=normal appearing spinal cord near affected cervical spinal cords, NCSC=normal cervical spinal cords.

$P < .017$ was considered to have statistical significant difference by using Calibrate the Chi-square test.

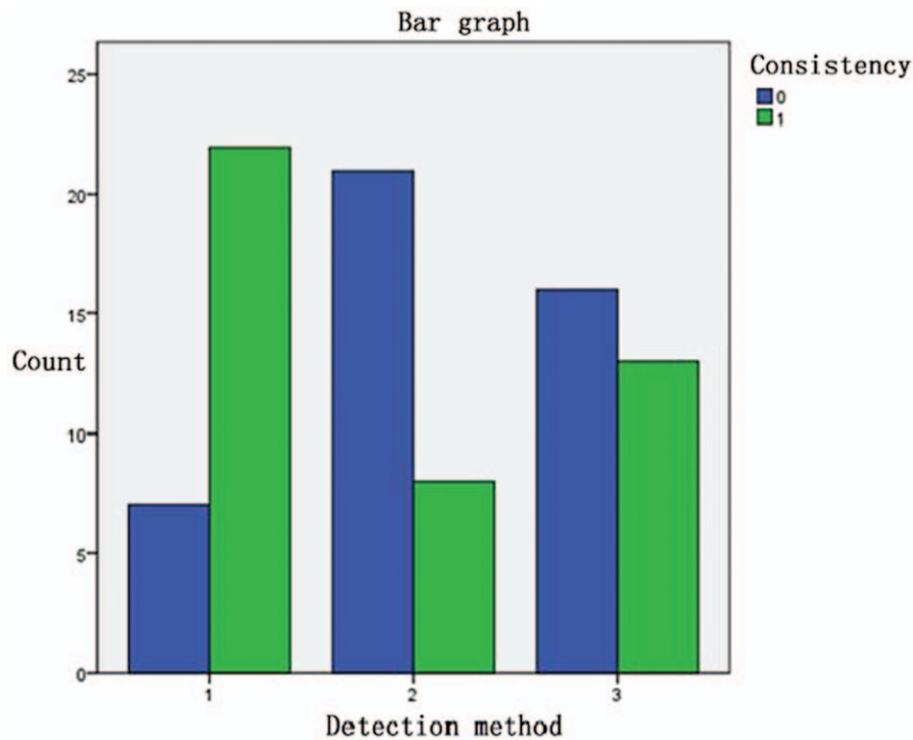


Figure 2. The consistency and comparison of MK, MD, and FA values in normal appearing spinal cords adjacent to the affected cervical spinal cords. The cut-off values of MK, MD, and FA of affected cervical spinal cords were obtained with receiver-operating characteristic (ROC) curve analysis; each of raw data was compared with the cut-off values for Consistency Checking. MK values had higher concordance in normal appearing spinal cords adjacent to the affected cervical spinal cords than MD and FA values. Notes: 1: MK value 2: MD value 3: FA value. FA = fractional anisotropy, MD = mean diffusivity, MK = mean kurtosis.

behavior in vivo tissue deviates from a Gaussian form due to complex cellular structures of tissue with many diffusion barriers like membranes, organelles, and water compartments.^[4,14] The diffusion kurtosis can be used to quantify the deviation from Gaussian distribution and also acts as an indicator for the complexity of microstructure.^[4] Thereby, DKI is considered to be more sensitive in detecting microstructural changes than conventional diffusion weighted and tensor imaging.^[6] By acquiring data for at least 2 nonzero diffusion gradient factors (b value) in more than 15 nonlinear directions, MK and conventional diffusion metrics (including MD and FA) are obtained simultaneously. MK is the average kurtosis of all diffusion directions. MK value is a new parameter in addition to the diffusion coefficient (FA and MD), measured by using higher b -value than conventional diffusion weighted and tensor imaging.^[15] The highest b -value applied in this study was 2000 s/mm^2 . MK was found to be able to reflect changes of cerebral infarction, multiple sclerosis and spondylotic myelopathy at an early clinical stage, and so on.^[3,14,15-20] In our study, Mean MK value in normal appearing spinal cords adjacent to the affected cervical spinal cords was significantly lower than mean MK value in normal cervical spinal cords. However, there was no significant difference in FA value and MD value. Therefore, MK value was more accurate compared to MD value and FA value in reflecting changes in microstructure of normal appearing spinal cords adjacent to the affected cervical spinal cords. It suggests that MK value could be a more sensitive metric for evaluating the changes of spin cord than MD and FA. Decreased MK value of cervical spinal cord adjacent to the lesion maybe caused by

Demyelination, Degenerative change, Microcirculation disorders, or Neuronal Atrophy.^[9,21-23]

MK is shown to be the most promising imaging markers as a nature indicator of tissue microstructure properties in the present study. A series of changes caused by Demyelination, Degenerative change, Microcirculation disorders and Neuronal Atrophy cause the heterogeneity and complexity of microstructure. MK value is more sensitive and accurate for the detection of microstructural changes, hence, these changes can be detected by MK at the early stages but are not sufficiently evident enough for MD or FA to recognize them. Therefore, MK could be used as another effective parameter for evaluating extensive cervical spinal cord damage in patients with cervical spondylotic myelopathy.

In this study, there was little limitations. First, the image time increased by adding the DKI sequence compared to standard MR sequences and some patients could not tolerate it. Second, this was a single institute study and the total amount of patients was relatively small which may introduce a statistical deviation. Therefore these results are preliminary and need to be confirmed by further investigation.

5. Conclusions

In conclusion, these results demonstrate significant differences in mean MK values between normal appearing spinal cords adjacent to the affected cervical spinal cords and normal cervical spinal cords. It is better to evaluate microstructural changes in cervical spondylotic myelopathy by mean MK instead of conventional diffusion weighted and tensor imaging parameters.

This new technique can be used as a biomarker for evaluating microstructural changes in cervical spondylotic myelopathy.

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