Effectiveness of Diffusion Tensor Imaging in Determining Cervical Spondylotic Myelopathy

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ABSTRACT

AIM: To determine the effectiveness of diffusion tensor imaging (DTI) in diagnosing cervical spondylotic myelopathy (CSM) in patients with no findings detected in conventional magnetic resonance imaging (MRI).

MATERIAL and METHODS: Fifty-four patients who presented for cervical MRI between January 2016 and June 2016, with symptoms such as neck pain, paresis, and numbness in hands, were included in the study. The patients were split into four groups based on their degrees of spinal stenosis. The obtained data were examined using special software and color-coded fractional anisotropy (FA), and apparent diffusion coefficient (ADC) maps were formed. Through these maps, using regions of interest (ROIs), FA and ADC values were calculated and the contribution of these values to the diagnosis was evaluated statistically.

RESULTS: When all grades of cervical spinal canal stenosis were compared, a statistically significant negative correlation between spinal canal stenosis degree and FA values, and a positive correlation between stenosis degree and ADC values were noted (p<0.001). In the comparison of stenotic levels and non-stenotic levels for the grade 2 patient group, there was a statistically significant decrease in FA values and an increase in ADC values in stenotic levels compared with prestenotic and poststenotic levels (p<0.05).

CONCLUSION: DTI and quantitative FA and ADC measurements are candidate imaging techniques for the diagnosis of early-stage CSM, which shows no findings in conventional MRI, and determining the degree of spinal cord injury.

KEYWORDS: Cervical spondylotic myelopathy, Diffusion tensor imaging, Fractional anisotropy, Apparent diffusion coefficient

■ INTRODUCTION

Cervical spondylotic myelopathy (CSM), which generally develops due to degeneration of the cervical spine, is the most common spinal cord disease in the population aged over 50 years (17). It is also the most common cause of non-traumatic spastic paraparesis and tetraparesis (2). Degeneration of cervical spinal elements is the primary pathologic lesion in cervical spondylosis, and secondarily, it causes the emergence of myelopathy symptoms through pressure on the spinal cord and/or vascular structures (19). Although high signal intensity in T2-weighted sequences on

magnetic resonance imaging (MRI) is an important tool for the diagnosis of CSM, this diagnosis is based primarily on clinical findings. However, some patients with CSM may show no findings in MRI (6,13,14).

Computed tomography (CT), CT myelography, and MRI methods are used in the diagnosis of CSM (8,22). The most commonly used imaging method is MRI, which is the most accurate radiologic examination method for detecting anatomic details, especially with regards to the brain. However, although MRI has a high sensitivity for anatomic details and pathology, it fails to show physiologic and metabolic changes

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in tissues (24). Recent innovations in neuroradiology have enabled us to produce physiologic maps alongside anatomic details (18). One of these new imaging techniques is diffusion tensor imaging (DTI). DTI is based on the determination of the structure of the tissue by measuring the in-vivo diffusion rate and direction of flow of water molecules. Diffusion-weighted MRI presents the diffusion speed of molecules in a single direction. Diffusion tensor MRI provides to determine the movement direction of molecules along with the speed of molecules. DTI is a modality where anisotropic diffusion is shown noninvasively. Anisotropic diffusion is displayed with constant indices such as fractional anisotropy (FA) (3,7).

The aim of this study was to determine the effectiveness of DTI in detecting CSM in patients whose clinical diagnosis is hard to be made in the early stage. The diagnosis can be overlooked due to confusion with radicular/nerve root involvements, and also patients have no findings in conventional MRI. Moreover, another goal was to foresee the path that leads to CSM in patients without clinical findings, by looking at whether there were correlations between spinal canal stenosis degree, FA, and apparent diffusion coefficient (ADC) values.

■ MATERIAL and METHODS

Patients

The study included 54 patients (19 men, 35 women) who were admitted to our clinic between January 2016 and June 2016 for cervical spinal MRI with a pre-diagnosis of cervical disc hernia/cervical myelopathy due to symptoms such as neck pain, paresis, and numbness in the hands. Spinal stenosis was graded in accordance with the classification in Figure 1A-D (5). The modified Japanese Orthopedic Association (JOA) score of the grade 2 patient group in our study was between 7-15, and the symptom duration of these patients

was longer than 6 months. The patients were subjected to DTI after implementation of three sequences (T1 and T2 sagittal, axial proton density) of routine imaging in the neutral position.

The exclusion criteria of our study were patients aged under 18 years, patients who had previously undergone surgery for cervical discopathy, patients with neurologic diseases that might cause symptoms of cervical myelopathy, patients with a pathology in the spinal cord (e.g. mass, myelitis, multiple sclerosis plaques), patients who could not tolerate additional MRI sequences, and patients who chose not to participate in the study voluntarily.

Imaging Protocol

All imaging was performed using a 1.5 Tesla MRI system (Siemens Vision-Symphony Upgrade, Erlangen, Germany) with a cervical spinal coil. Patients were not subjected to any preliminary preparation. DTI was conducted after obtaining consent forms from the patients, after conventional routine MRI consisting of three sequences (T1 and T2 sagittal, axial proton density).

DTI was obtained using single-shot spin-echo planar image (SS-SE-EPI) after applying an anterior double saturation band in order to prevent artifacts. Image parameters: TR (time to repeat): 2300 ms; TE (time to echo): 94 ms; FOV (field of view): 230 mm; matrix: 128x128; slice: 3.5 mm; gap=0. Two series of diffusion-weighted images were obtained, with a b factor of 0-1000 in each direction, and a gradient was used towards 16 different directions. The duration of DTI was approximately 7.5 minutes.

Image Assessment and Analysis of Regions of Interest (ROI)

First, conventional MRI sequences were obtained, followed by DTI sequences. The conventional MRIs were analyzed to
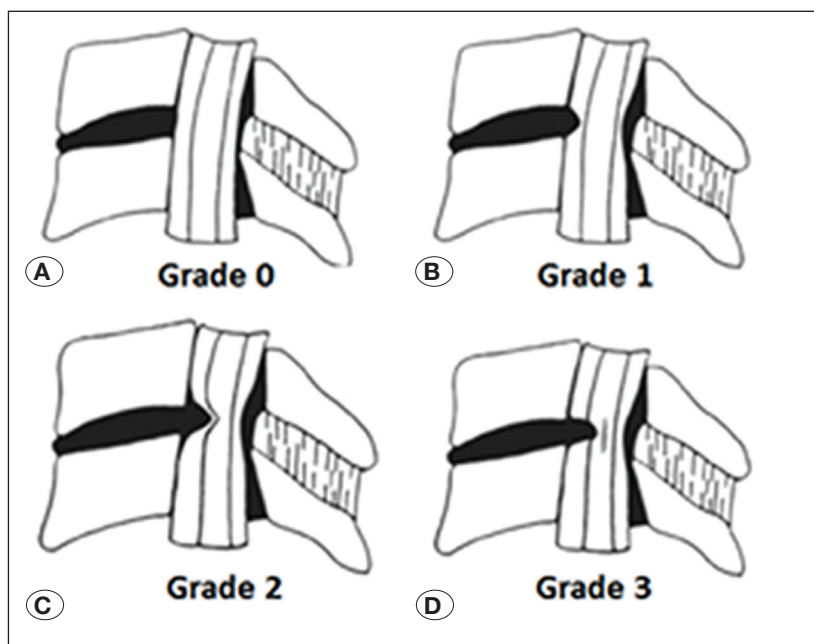
Figure 1A-D: Schematic view of the degree of cervical canal stenosis (5). **(A)** Grade 0: normal. **(B)** Grade 1: more than 50% obliteration of the subarachnoid space without deformation in the cord. **(C)** Grade 2: deformation in the spinal cord without signal increase. **(D)** Grade 3: signal increase for spinal cord, on T2-weighted images.

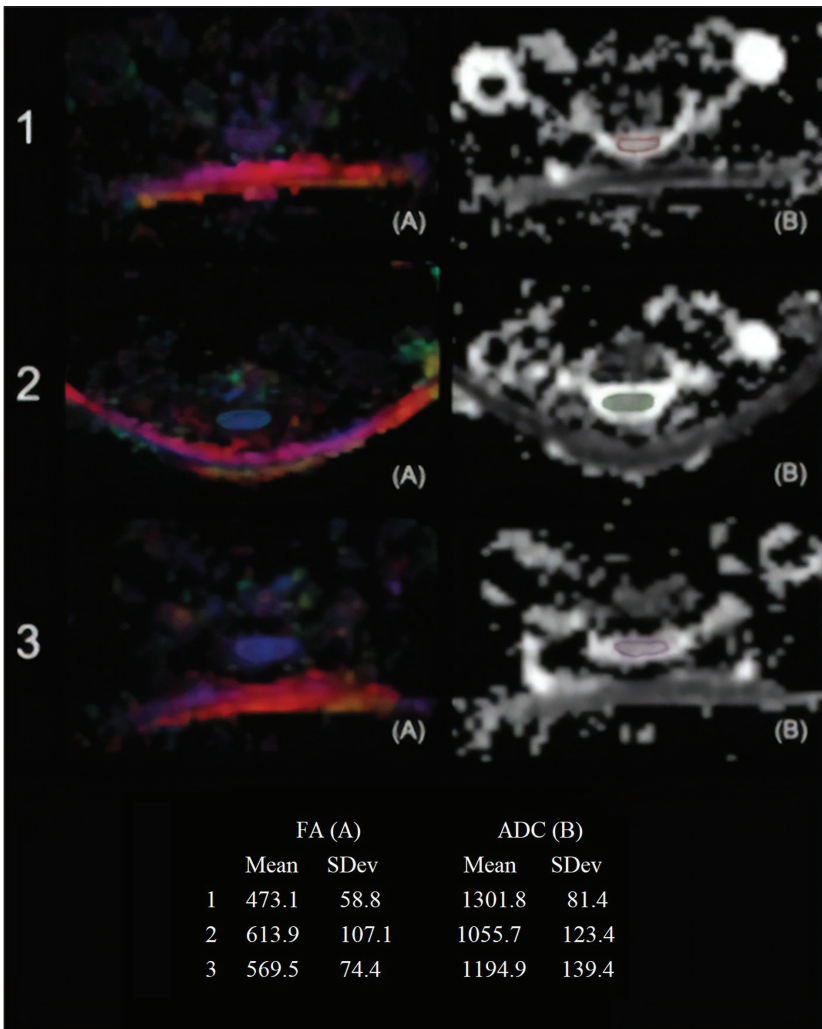see whether patients had spinal cord tightness caused by spondylotic changes, and if so, to what degree.

DTI images were transferred to the workstation (Leonardo Workstation) and analyzed using special software (Syngo MMWP), and FA and ADC maps were automatically produced from this DTI source, using the same software. FA and ADC measurements were obtained manually using the ROI method over trace-weighted images because they show spinal cord boundaries better. During ROI measurements, care was taken to exclude cerebrospinal fluid (CSF) and to avoid the partial volume effect. The ROI we obtained included both gray and white matter. Although the isotropic diffusion properties of grey matter and the high anisotropic diffusion properties of white matter would affect FA and ADC values, we preferred to work with a single ROI with as wide a scope as possible without exceeding cord boundaries. The reason behind this preference was to ensure that the procedure was simple and minimally dependent on the practitioner in clinical routine practice. For patients with spinal canal stenosis, measurements were made from stenotic, prestenotic, and poststenotic levels in the axial slices (Figure 2). In normal patients (grade 0) without spinal canal stenosis, measurements were made at the lower and upper two cervical levels as cervical (C) 2-3 and C 5-6 in axial sections and averaged.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 15 program. While analyzing the study data, Student's t-test was used to evaluate quantitative data besides descriptive statistical methods (mean, standard deviation). In comparisons of more than two groups, one-way analysis of variance (ANOVA) was used, followed by the Tukey test for differences between the groups. The relation between the quantitative values was examined using Pearson's correlation coefficient. The results were evaluated at 95% confidence intervals and a significance level of $p < 0.05$.

Additionally, receiver operating characteristics (ROC) curve analysis was performed to measure the effectiveness of FA and ADC values on diagnosing cervical spondylotic myelopathy in the patient group. In order to estimate different models, the area under the ROC curve (AUC), cut-off points, and sensitivity and specificity values were assigned.

	FA (A)		ADC (B)	
	Mean	SDev	Mean	SDev
1	473.1	58.8	1301.8	81.4
2	613.9	107.1	1055.7	123.4
3	569.5	74.4	1194.9	139.4

Figure 2: 1A, B – 3A, B: Measurement of FA and ADC values, with a manually drawn ROI at the stenotic, prestenotic, and poststenotic levels, of a 55-year-old patient with grade 2 stenosis. **1A, 1B** show measurements by ROI in axial color-coded FA and ADC maps at the stenotic level, **2A, 2B** at the prestenotic level, and **3A, 3B** at the poststenotic level. Their measurements are displayed with ROI in axial color-coded FA and ADC maps. FA and ADC values in these levels are displayed below in the table respectively.

■ RESULTS

A total of 54 patients between the ages of 20 and 80 years, 35 females (65%) and 19 males (35%), were included in the study. The spinal canal stenosis degrees of all patients were classified according to the grading system in Figure 1A-D. Nine of 54 patients were evaluated as grade 0, 11 as grade 1, 22 as grade 2, and 12 as grade 3. In our study, the mean FA and ADC values at the most stenotic level in patients with stenosis grade 1, 2, and 3 were compared with the mean FA and ADC values in normal patients (grade 0). In addition, in the grade 2 patient group with no deformation in the spinal cord and no signal change, FA and ADC values at the stenotic level were compared with the prestenotic and poststenotic levels.

The mean and standard deviation of FA and ADC values are shown according to grades (Table I). In the comparison of measurements of FA values at the most stenotic levels in patients with grade 1, 2, and 3 stenosis and the normal (grade 0) group, no statistically significant difference in FA values between patients who were grade 1 and normal patients was captured (p=0.283); however, a significant decrease in FA

values was detected in the comparison of patients who were grade 2 and grade 3 and the normal group (p<0.05). Moreover, a negative correlation was found between FA values and the degree of central canal stenosis (Figure 3). When ADC values at the stenotic level between the normal group (grade 0) and other groups (grades 1, 2, and 3) were compared, a significant increase in ADC values for patients who were grade 3 was detected compared with the normal group, whereas there was no statistically significant difference between grade 1, grade 2, and the normal group (grade 0). In the correlation evaluation, there was an increase in ADC values compared with grades and a positive correlation was observed (Figure 4).

Mean and standard deviation values of stenotic, prestenotic, and poststenotic FA and ADC values in patients with grade 2 stenosis are shown in Table II. FA values show a statistically significant decrease at the stenotic level compared with the prestenotic and poststenotic levels (p<0.05). In addition, a statistically significant increase in ADC values at the stenotic level compared with the prestenotic and poststenotic levels was observed (p<0.05).

**Table I:** Mean ± Standard Deviation of FA and ADC Values, in accordance with the Grades

Grade	FA	ADC
Grade 0 (normal)	0.62 ± 0.019	1.04 ± 0.055
Grade 1	0.59 ± 0.055	0.96 ± 0.29
Grade 2	0.52 ± 0.039	1.12 ± 0.102
Grade 3	0.40 ± 0.055	1.35 ± 0.189

Table II: Mean ± Standard Deviation of FA and ADC Values in Grade 2 Patient at the Prestenotic, Poststenotic, and Stenotic Levels

	FA	ADC
Prestenotic	0.63 ± 0.024	0.97 ± 0.069
Stenotic	0.52 ± 0.039	1.12 ± 0.102
Poststenotic	0.57 ± 0.047	1.01 ± 0.063
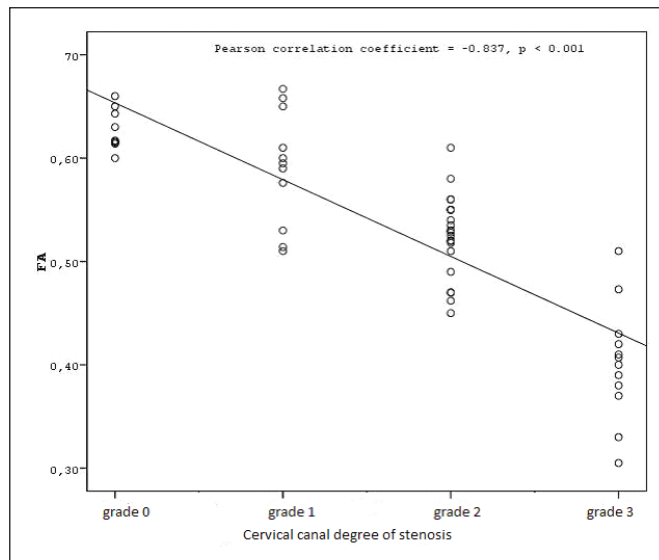
Figure 3: The relation between the degree of central canal stenosis and FA values. A negative correlation was determined between the degree of central canal stenosis and FA values. A negative correlation was found between FA values and the degree of central canal stenosis.
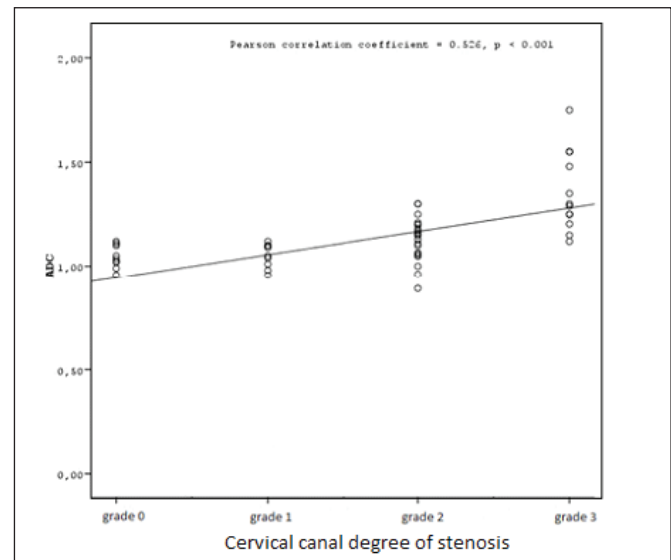

Figure 4: The relation between the degree of central canal stenosis and ADC values. A positive correlation was found between ADC values and the degree of central canal stenosis.

In the ROC analysis at stenotic level for the grade 2 group, to detect deformations in the spinal cord structure, sensitivity and specificity of FA values were found as 95% and 78%, respectively, when the cut-off value of FA was taken as 0.456. The sensitivity and specificity of ADC values were found as 63% and 36%, respectively, with a cut-off value of 1.105. The ROC test results yielded AUC values in FA [0.964 (0.907-1.021)] and ADC [0.136 (0.005-0.226)] (Figure 5).

■ DISCUSSION

T2 signal increase on MRI is a symptom of CSM that occurs at the late stages of disease, and accepted as an indication of poor neurologic outcome, even after surgery (2,21). On the other hand, early radiologic diagnosis of CSM is important for early initiation of treatment and obtaining good results from treatment (2,15,16). In conventional MRI evaluations of patients with a clinical diagnosis of CSM, sensitivity was found between 15-65% (12,14). The failure of routine MRI to show early changes in spinal segments retained for CSM and microstructural features of the spinal cord has prompted the requirement for new imaging techniques that can be used to detect early spinal cord changes prior to T2 signal increase (4,11). In this respect, DTI, which measures the diffusion rate and direction of intracellular and extracellular water molecules, can be used for this purpose because it shows the microscopic structural organization of white matter fibers. Diffusion-weighted MRI shows the diffusion rate information of molecules in one direction. In DTI examinations, the direction of movement along with the speed of the molecules is determined. The assumption on the basis of DTI is that the Brownian movement of free water protons, with different speeds in different tissues, is restricted more in the perpendicular direction to myelin-rich axons compared with the parallel direction myelin-rich axons in brain tissue. In white matter pathways, features such as axon density, mean axon diameter, myelin sheath thickness, and orientation of pathways affects the diffusion in that tissue and gives us important information about the structure of pathways (9).
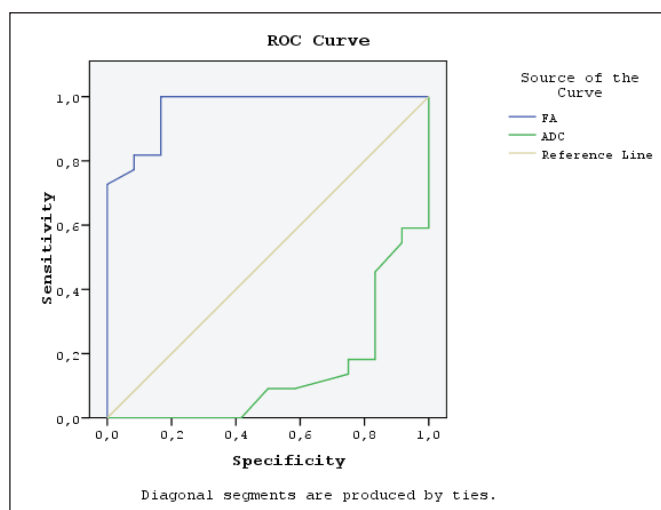
Figure 5: ROC curve analysis in the grade 2 patient group to detect cervical spondylotic myelopathy.

If the structure of the spinal cord tracts deteriorates, as in CSM, the movement of water molecules in the direction of the corridor increases. In this case, anisotropic diffusion values and FA decrease, whereas isotropic diffusion and ADC increase (10,26).

The use of DTI in the spinal cord has several difficulties. Besides the complex anatomic location of the cord and its thin structure, there is an increased sensitivity artifact due to motion artifacts and CSF pulsation. Wilm et al. managed to reduce artifacts and optimize images by taking oblique spin echo using a small FOV and saturation band (25). Similarly, we tried to reduce artifacts as much as possible using a small FOV and double saturation band. Song et al. compared conventional MRI and DTI in 53 patients with CSM and 20 healthy volunteers; only 24 patients with T2 signal change showed high signals in the cervical cord; no abnormalities were detected in the remaining 26 individuals. DTI maps showed cervical spinal abnormalities in 39 patients. They found a high signal in ADC, a low signal in FA, and a patchy yellow signal in colored DTI maps, unlike the spinal cord that normally appears blue. DTI can detect more pathology than conventional MRI, and it is concluded that patients with CSM have high ADC and low FA values compared with normal individuals (20). In another study by Toktas et al. with 21 patients showing CSM signs and symptoms but without T2 signal change, it was noted that there was a statistically significant decrease in FA values at the stenotic level compared with the nonstenotic level and a significant increase in ADC values (23). Similar results were found in the study of Ahmadli et al. (1).

Our findings are similar to the above-mentioned studies; in the grade 2 patient group with CSM symptoms but no conventional T2 signal change in conventional MRI, there was a significant decrease in FA values at the stenotic level compared with prestenotic and poststenotic levels, and a statistically significant increase in ADC. In addition to the previous studies, in our study, by examining all degrees of cervical stenosis and normal patients, we found that as the degree of cervical stenosis increased, FA values showed a negative correlation, and ADC values showed a positive correlation. Finally, in our study, we calculated cut-off values, which were not determined in previous studies. An FA cut-off below 0.456, and ADC cut-off above 1.105 can detect CSM. Moreover, we found that the FA value was a more sensitive examination method compared with ADC, by considering its cut-off value and its higher sensitivity and specificity for the detection of CSM.

One of the limitations in our study was that our patient groups were not numerically homogeneous. Another limitation is that no comparison could be made in terms of clinical improvement due to the lack of follow-up time and lack of control radiologic examinations in our grade 2 study group with a modified JOA score of 7-15. For instance, re-evaluation of DTI values of patients treated conservatively could show the effectiveness of the treatment method. Also, due to the absence of follow-up examinations, comparisons of JOA scores of non-surgical patients with grade 2 stenosis and radiologic change levels could not be made, and it is not known whether T2 signals change over time.

■ CONCLUSION

Our findings show that DTI is valuable in demonstrating microstructural and molecular level changes in the spinal cord of patients with CSM without pathologic signal change and significant clinical deterioration. FA and ADC values used in DTI can help to determine the degree of spinal cord damage resulting from compression due to degenerative spondylosis. Moreover, with DTI, diffusion abnormalities in compression areas without T2 signal change can be detected in conventional MRI. In order to provide better clinical results and early intervention in patients with CSM, DTI values can be put into routine use after more comprehensive and long-term studies.

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