

Original Article

Diffusion tensor imaging of cervical spinal cord: A quantitative diagnostic tool in cervical spondylotic myelopathy

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Abstract

Background: Diffusion tensor imaging (DTI) is a novel magnetic resonance imaging (MRI) technique potentially able to evaluate the microscopic structural organization of white matter fibers. **Aim:** This study aimed to compare fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values obtained by DTI in stenotic versus nonstenotic cervical spinal segments of patients with clinical and neurological evidence of cervical spondylotic myelopathy (CSM). **Materials and Methods:** This prospective study included 21 patients with CSM but without T2 changes on conventional MRI. Diffusion tensor (DT) images from the stenotic and nonstenotic segments of the subjects were obtained. FA and ADC values were estimated and compared with stenotic versus nonstenotic segments. **Statistical Analysis:** Paired *t*-test was used [Statistical Package for the Social Sciences (SPSS) 12.0]. **Results:** In the most stenotic segments, the mean FA value was significantly lower (0.4228 ± 0.1090 vs 0.6884 ± 0.0075 , $P < 0.001$) and the mean ADC value was significantly higher (1.312 ± 0.2405 vs 0.9183 ± 0.1477 , $P < 0.001$) when compared to nonstenotic segments. In addition, there was a negative correlation between FA and ADC values ($r = 0.63$, $P = 0.002$). **Conclusions:** DTI of the cervical spine seems to be a promising novel imaging modality in patients with CSM. **Advances in Knowledge:** DTI may offer increased diagnostic sensitivity as compared to standard MRI and enables earlier detection of the disease.

Key words: Apparent diffusion coefficient (ADC), cervical spondylotic myelopathy (CSM), diffusion tensor imaging (DTI), fractional anisotropy (FA)

INTRODUCTION

Cervical spondylotic myelopathy (CSM) is the most common type of acquired spinal cord dysfunction,^[1] affecting more than 60% of the population over 40 years of age.^[2] It generally develops

over the years as a result of thickening and calcification of the posterior longitudinal ligament causing segmental compression of the spinal cord.^[3,4] In subjects with CSM, major mechanisms

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responsible for the spinal cord injury include the spinal cord ischemia and microtrauma. Characteristic magnetic resonance imaging (MRI) findings suggestive of CSM, such as increased signal intensity of the spinal cord on T2-weighted imaging, typically occur late in the course of the disease and are predictive of poor neurological outcome even with decompression surgery.^[5,6] Unfortunately, conventional MRI for the evaluation of CSM shows a poor correlation with the symptoms and prognosis, as suggested by the results of clinical studies showing a diagnostic sensitivity between 15% and 65% in patients with major signs and symptoms of CSM.^[7-10] On the other hand, prompt diagnosis of CSM is clinically important, as early initiation of treatment yields better outcomes in these patients.^[7,11-16]

The failure of routine magnetic resonance (MR) imaging to demonstrate early microstructural changes in the involved spinal segments warrant alternative or novel neuroimaging modalities that are able to detect early spinal cord changes before the development of T2 hyperintensity.^[17,18] In this regard, diffusion tensor imaging (DTI) represents a relatively novel MRI technique sensitive to the diffusion of water molecules within and across the intra- and extracellular spaces of tissues allowing the calculation of a variable, referred to as diffusion tensor (DT), which is able to reflect the microscopic structural organization of white matter fibers on a macroscopic scale (voxel size of the order of a few mm³).^[19]

Objective measurements provided by DTI such as fractional anisotropy (FA) and apparent diffusion coefficient (ADC) could help elucidate the degree and chronicity of spinal cord disease resulting from compression caused by degenerative spondylosis. DTI can also detect diffusion abnormalities in areas of spondylotic compression without T2 signal change on conventional MRI.^[20] In a normal resolution of a DT-MRI experiment (2-3 mm voxel sizes), the diffusion-weighted signals of the gray matter and cerebrospinal fluid do not change according to the direction in which the gradients are applied, and the diffusion appears isotropic.^[21]

Within the white matter, water molecules diffuse more freely along the dominant fiber orientation as compared to the direction across them. Such an anisotropy of diffusion provides insights into the microstructural organization of the white matter^[22] and the simplest model that represents this anisotropic diffusion is the diffusion tensor. Application of diffusion gradients in six noncollinear and noncoplanar orientations allows the estimation of the six unknown elements of the diffusion tensor^[23] and thus, characterizes the anisotropy.

Furthermore, the direction with the greatest attenuation of the diffusion-weighted signal gives an indication of the dominant fiber orientation, which then can be used to create voxelwise maps of fiber orientation or can be pieced together to reconstruct continuous trajectories throughout the white matter (i.e., “tractography”).^[22]

This study aimed to compare FA and ADC values obtained by DTI in stenotic versus nonstenotic cervical spinal segments of

patients with clinical and neurological evidence of CSM but without T2 changes on conventional MRI in an attempt to explore the potential role of DTI in early detection of possible spinal cord damage.

MATERIALS AND METHODS

Subjects

Twenty-one consecutive patients (12 males, 9 females; mean age: 53.8 years with a range between 36 years and 69 years) with cervical compressive myelopathy were prospectively studied from January 2011 to September 2011. Each subject underwent comprehensive physical and neurological examinations by a neurosurgeon and a neurologist from the research team, and the diagnosis of cervical compressive myelopathy was established based on the clinical manifestations (neck pain, extremity numbness, walking difficulty, etc.) of the patients, all of whom had MRI findings consistent with cervical canal stenosis with calcification or thickening of the ligamentum flavum without signal changes in spinal cord on T2-weighted images.

Exclusion criteria included increased signals on T2-weighted images of the cervical spinal cord, previous spinal surgery, history of cervical trauma, stroke, and/or other neurological disease(s), cervical radiculopathy with no clinical evidence of cervical myelopathy, absence of radiological evidence of cervical canal stenosis, and contraindication to MRI (including severe claustrophobia).

FA and ADC values of upper nonstenotic cervical segments (C2-C3) were used as controls since as was previously shown, no difference in FA and ADC existed between segments in healthy controls and nonstenotic segments of subjects with cervical spinal stenosis.^[24]

Magnetic resonance imaging protocol

MRI examinations were performed on a 1.5-T MRI system (Siemens MAGNETUM Espree, Erlangen, Germany) with a protocol routinely including sagittal T2-, sagittal T1- and T2 axial-weighted fast spin echo (FSE) sequences, and a 20 direction echo planar imaging (EPI)-based DTI sequence in an axial plane. For conventional sequences, scanning orientations were sagittal T1-weighted image, sagittal T2-weighted image, and axial T2-weighted image. The images were obtained with a field of view (FOV) of 240 mm for sagittal scanning and 180 mm for axial scanning, and an image matrix was 320 × 240 for axial scanning and 448 × 246 for sagittal scanning. The conventional MRI sequences were fast-spin-echo T1-weighted sagittal image (TR/TE = 516 ms/9.8 ms), T2-weighted sagittal image (TR/TE = 2000 ms/123 ms), and gradient echo (GRE) T2-weighted axial image for intervertebral disc space (TR/TE = 659 ms/20 ms). Slice thickness was 3 mm, and slice gap was 0.3 mm and number of acquisition was 2. Parameters for DTI were obtained as follows: Using axial plane, slice thickness was 4 mm, slice gap was 1 mm, slice number was 30, acquisition matrix was 128

× 128, FOV was 230 mm, and number of acquisitions was 3. Diffusion was measured along 20 noncollinear directions with two b values (0-1,000 s/mm²).

Image processing and data analysis

Acquired DTI images were processed using the MR scanners 3D software (Syngo, Siemens Medical Solutions), to produce ADC and FA maps of the acquired axial slices. The anisotropic diffusion in the anteroposterior direction was shown in red, the craniocaudal direction was shown in blue, and the right-left direction was shown in green on colored FA maps [Figure 1]. The ADC and FA values were measured using regions of interest technique in the cervical spinal cord at nonstenotic C2-3 and at the most stenotic segment [Figure 2]. Since the cross-sectional area of the spinal cord was different in stenotic and nonstenotic segments, the sizes of the regions of interest (ROIs) were not always the same in stenotic and nonstenotic segments as well as in diseased segments and control segments, ranging between 45 mm² and 60 mm².

Statistical analyses

A standard Statistical Package for the Social Sciences (SPSS) 12.0 (SPSS Institute, Chicago, IL, USA) software package for Windows was used for the statistical analyses. Paired *t*-test was used to compare FA and ADC values of the spinal cord in stenotic and nonstenotic segments. Correlation analysis was performed between FA and ADC values. A *P* value below 0.05 was considered to be “statistically significant.”

RESULTS

The mean FA and ADC in the most stenotic cervical segment were 0.4228 ± 0.1090 and 1.312 ± 0.2405 (in 1×10^{-3} mm²/s), respectively. The mean FA and ADC values in the nonstenotic upper cervical segments were 0.6884 ± 0.0075 and 0.9183 ± 0.1477 (in 1×10^{-3} mm²/s), respectively.

There was a significant decrease in FA and significant increase in ADC in the stenotic segments ($P < 0.001$). A negative

correlation was found between FA and ADC values ($r = 0.63$, $P = 0.002$).

DISCUSSION

Spinal cord ischemia and microtrauma are the major mechanisms responsible for the spinal cord injury in CSM. Conventional MRI findings such as increased signal intensity on T2-weighted images indicative of myelomalacia typically occur late in the disease process and predict poor neurological outcome even with decompression surgery.^[5,6] In this regard, the timing of surgery is also important since early surgical treatment yields better outcomes,^[7,11-16] underlying the importance of early radiological diagnosis of CSM.

Thanks to its high soft tissue resolution, conventional MRI plays a major role in delineating the anatomical structure and diagnosing numerous pathological conditions of the spinal cord including cervical canal stenosis, herniation of the intervertebral disk, thickening of the ligamentum flavum and the posterior longitudinal ligament, myelomalacia, neoplasias, and inflammation. However, since conventional MR images are not able to reveal the microstructural characteristics of the spinal cord, including the fiber tract of the white matter, alternative approaches such as the “diffusion-tensor imaging” has been developed, which may enable detailed *in vivo* analysis of the diffusion of water molecules.^[25]

Conventional MRI utilizes isotropic diffusion parameters based on water diffusion, which is equal in all directions, and it is quantified by the “apparent diffusion coefficient.” Conventional MR images are “pictures” primarily of free water, the concentration of which differs by tissue type. For instance, white matter is composed of about 70% water while the corresponding figures for gray matter and CSF are around 80% and 99%, respectively. These differences in water content contribute to the contrast between tissue types visible on structural images.^[26]

In contrast, DTI is based on anisotropic diffusion parameters describing highly ordered water movements occurring along a

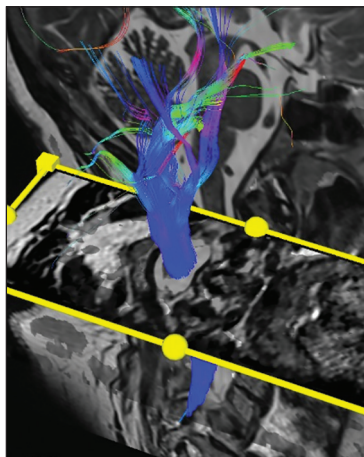


Figure 1: 3D reconstruction of spinal cord fiber tracts in colored FA maps

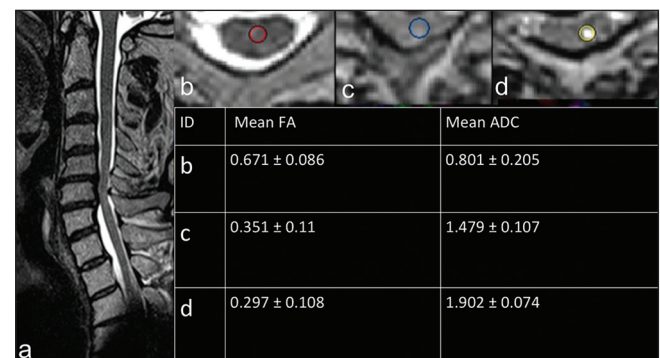


Figure 2: (a) Cervical MRI in the sagittal plane showing cervical stenosis at C5 and C6. Axial T2-weighted images where mean FA and mean ADC values are measured at specific ROI from nonstenotic cervical segment (b), from stenotic cervical segments (c), and from myelomalacic cervical segment (d)

single direction and it takes conventional MRI one step further by measuring differences in the amount and orientation of water diffusion, particularly in the white matter.^[26] Anisotropic diffusion is quantified by FA, which is a diffusion index measuring the degree of order in water diffusion where a value of 0 represents isotropic diffusion and 1.0 represents complete anisotropic diffusion.^[27] In physiological conditions, water molecules in spinal tracts travel in a highly ordered fashion mostly in a single direction, rendering FA closer to its highest value. However, if tracts are distorted, such as the case in cervical spondylotic myelopathy, water molecules rather tend to move in all directions instead of going only up and down. In that situation, anisotropic diffusion and FA value decreases, whereas isotropic diffusion and ADC value increase.^[28,29]

In this regard, in a study by Dousset *et al.*, the superiority of DTI over T2-weighted imaging in patients with CSM was shown.^[30] One of the first reports on the use of DTI modality in CSM patients was conducted by Demir *et al.*^[31] Song *et al.* compared DTI and conventional MR in 53 CSM patients and 20 healthy volunteers^[3] and demonstrated high signal intensity within the cervical cord in 24 only cases with conventional T2-weighted images; no abnormalities were found in the remaining 26 subjects (three cases were excluded from the study due to low quality MR images). On the other hand, DTI maps showed the following signal abnormalities in the cervical spinal cord in 39 cases: high signal intensity on ADC, low signal intensity on FA, and patchy yellow signal on color DTI maps appearing on an otherwise normal blue spinal cord. The authors concluded that color DTI was able to detect more lesions than routine MRI and that significantly higher ADC and lower FA values were present in CSM patients as compared to healthy individuals. In a recent study, a significant relation was proposed between DTI findings and clinical parameters in patients with cervical myelopathy.^[32] In another study by Kara *et al.*, a total of 16 patients with neurological signs and symptoms of CSM but without hyperintensity in spinal cord on T2-weighted images were assessed. MRI examinations were performed on a 3-T MR imaging system. FA of the spinal cord at the stenotic level showed a statistically significant reduction while there was a statistically significant increase in the measured ADC.^[20]

Our findings are in line with the results of the abovementioned studies. According to our findings, the mean FA in stenotic segments (0.423) was significantly lower compared with nonstenotic segments (mean 0.688) and the mean ADC of stenotic segments ($1.313 \times 10^{-3} \text{ mm}^2/\text{s}$) was significantly higher as compared with the nonstenotic segments ($0.918 \times 10^{-3} \text{ mm}^2/\text{s}$).

However, the several limitations of our study should be mentioned. First, our sample population was relatively small and there was no long-term follow-up of our patients.

Also, the proposed association between FA and early stage CSM could only be proven if a majority of the patients went on to develop hyperintensity on T2-weighted images during the follow-up. However, all of the patients underwent surgery, which

required instrumentation for cervical stability, which precluded a DTI examination of the cervical spinal cord in these patients. A similar limitation has also been previously reported by Kara *et al.*^[20] Therefore, it is impossible to predict the percentage of our patients who would have developed T2 hyperintensity when left untreated.

CONCLUSIONS

T2 signal changes in conventional MR images in patients with CSM are associated with poor prognosis after surgery, underscoring the importance of early diagnosis and treatment in this condition. DTI of the cervical spine is a promising novel imaging modality in this group of patients offering increased diagnostic sensitivity as compared to standard MRI and enabling earlier detection of CSM before T2 changes appear on conventional MRI. Diagnostic improvements observed in these preliminary studies with the use of DTI warrant further studies with larger samples designed to evaluate the sensitivity and specificity of DTI in CSM in order to better identify patients at risk of progressive myelopathy.

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Conflicts of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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