



A preliminary study of 3.0-T magnetic resonance diffusion tensor imaging in cervical spondylotic myelopathy

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Abstract

Purpose To compare diffusion tensor imaging (DTI) parameters of the spinal cord between patients with cervical spondylotic myelopathy (CSM) and normal subjects, and investigate their significance in the clinical diagnosis, surgical planning and post-operative evaluation of CSM.

Methods Routine sequence magnetic resonance imaging (MRI) and DTI scans were performed in 50 normal subjects and 60 cases of CSM with 3.0-T MR. DTI images, apparent diffusion coefficient (ADC) and fractional anisotropy (FA) color-maps corresponding to spinal cord cross-sections were obtained. The spinal cord function of CSM patients was measured using modified Japanese Orthopaedic Association (mJOA) scoring and Nurick grade at different times. The changes in DTI parameters and their correlation with spinal cord function scores were analysed by SPSS 19.

Results There were significant differences in DTI parameters of the spinal cord between normal subjects and patients with CSM (ADC: 1.119 ± 0.087 vs. 1.395 ± 0.091 , $P < 0.01$; FA: 0.661 ± 0.057 vs. 0.420 ± 0.080 , $P < 0.01$). The FA values at the maximal compression level of the spinal cord in the patients with CSM were significantly associated with the mJOA score pre-operatively, 1 week, and 1, 3 and 6 months post-operatively, with Pearson's correlation coefficients of 0.58 ($P < 0.01$), 0.53 ($P < 0.05$), and 0.51 ($P < 0.05$), 0.54 ($P < 0.05$) and 0.55 ($P < 0.05$), respectively. However, the FA values were significantly negatively associated with the Nurick grade, with Pearson's correlation coefficients of -0.40 ($P < 0.05$), -0.39 ($P < 0.05$), and -0.41 ($P < 0.05$), -0.45 ($P < 0.05$) and -0.44 ($P < 0.05$), respectively.

Conclusions DTI may play a significant role in diagnosing and predicting the development of CSM.

Graphical abstract These slides can be retrieved under Electronic Supplementary Material.

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Key points

1. Cervical spondylotic myelopathy
2. Spinal cord
3. Magnetic resonance imaging
4. Diffusion tensor imaging
5. Spinal cord function scores

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Take Home Messages

1. DTI colormaps of spinal cord in patients with CSM can reflect compression and functional status of spinal cord.
2. The FA value of spinal cord was associated with post-operative recovery of spinal cord function.
3. DTI may play a significant role in diagnosing and predicting the development of CSM.

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Fulong Dong and Yuanyuan Wu contributed equally to this work and should be considered co-first authors.

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Extended author information available on the last page of the article

Keywords Cervical spondylotic myelopathy · Spinal cord · Magnetic resonance imaging · Diffusion tensor imaging · Spinal cord function scores

Introduction

Cervical spondylotic myelopathy (CSM) is the most common cause of cervical spinal cord dysfunction [1]. It is a progressive, degenerative spine abnormality, causing cervical spinal cord damage [2]. Among people above 40 years old, approximately 60% suffer from this disease [3]. Its pathological mechanisms include mechanical compression and secondary biological damage [4].

Imaging technology is an integral part of CSM patient management. The earliest imaging diagnosis of CSM began with the X-ray, CT and computed tomography myelography (CTM) on the morphological description of the cervical spinal canal. Some scholars have tried to determine cervical spinal cord compression by measuring the spinal canal parameters, thus providing imaging evidence for the clinical diagnosis of CSM [5–8]. Magnetic resonance imaging (MRI), which has changed the condition in which radiology solely relied on morphological changes to predict the diagnosis of the disease, became the most important imaging diagnostic methods for CSM [9]. However, traditional MRI has its limits in the prediction of neurological function, often underestimating the extent and severity of spinal cord injury [10]. Therefore, a new imaging technique that can clearly describe the function of the spinal cord is called for improving the promptness and sensitivity of diagnosis.

Diffusion tensor imaging (DTI) is a new magnetic resonance technique that emerged in recent years. Studies have shown that DTI can display the damage of the spinal cord before MR T2-weighted imaging (T2 WI) [11–13]. Therefore, DTI of the spinal cord marked a significant advancement in the field of neurological imaging, and its application will greatly expand the diagnosis and treatment evaluation of CSM.

In this study, we measured the DTI parameter of cervical spinal cord in normal subjects and CSM patients, and explore its correlation with clinical function scores.

Subjects and methods

Subjects

Fifty normal subjects were randomly sampled from healthy volunteers in whom a physical examination, X-ray and MRI were performed. Those with cervical diseases, such as cervical spine trauma, deformity and other cervical spine diseases were excluded. Normal subjects included 32 males

and 18 females, with a mean age of 45 years (22–74 years). Sixty patients with CSM were randomly sampled from those admitted to the hospital during a period from October 2013 to October 2016. All patients underwent physical examinations, X-ray and MRI scan, and patients with ossification of posterior longitudinal ligament (OPLL), amyotrophic lateral sclerosis (ALS) and spinal tumour were excluded. Of 60 patients, 39 were male and 21 were female, with a mean age of 55 years (35–82 years). Most patients were in a chronic process, and showed a progressive exacerbation. The duration of the disease ranged from 2 months to 16 years, with a mean of 4.6 years. After the onset of the disease, all subjects experienced neck and shoulder discomfort, numbness of limbs, unsteady gait and zonesthesia (a feeling or sensation of constriction in the body) in the chest or abdomen. Physical examination showed that compression was mainly on the lower cervical spinal cord, and different degrees of incomplete paralysis were detected in the limbs. In addition, there were obvious sensor and activity disorders in the limbs, and hyperreflexia was observed and the pathological tendon reflex was positive.

All patients with CSM underwent surgical treatment. According to the location and segment of spinal cord compression, different approaches (anterior, posterior or anterior–posterior) and techniques were chosen. The anterior approach in the study included anterior cervical discectomy and fusion (ACDF) and anterior cervical corpectomy and fusion (ACCF). The posterior approach was an open-door

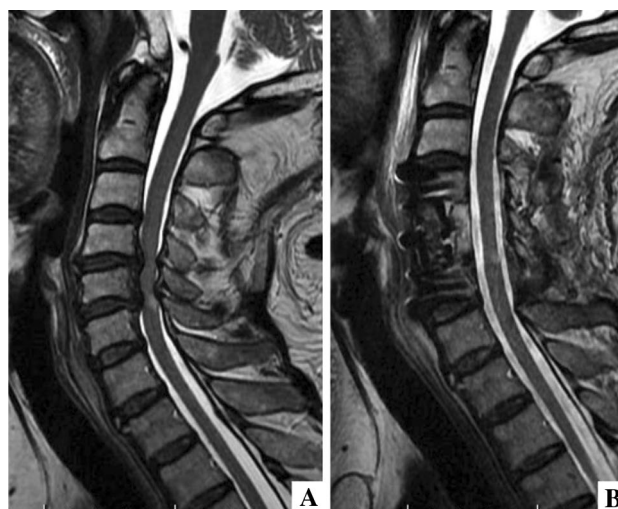


Fig. 1 Comparison of pre-operative and post-operative MRI in patients with CSM. **a** MR T2 WI of pre-operation; **b** MR T2 WI of post-operation

extensive laminoplasty. Pre-operative and post-operative MRI of patients with CSM is shown in Fig. 1. Cervical spinal cord function of patients with CSM was measured using the modified Japanese Orthopaedic Association (mJOA) scoring [14] and Nurick grade [15] method pre-operatively, 1 week, and 1, 3 and 6 months post-operatively (Table 1). The study was approved by the Ethics Committee of University and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from volunteers and patients.

Measurement methods

All MRI conventional sequence scans and DTI scans were performed on a GE Signa HDxt 3.0-T magnetic resonance machine (General Electric Company, USA). Subjects were in supine position, wore earplugs, and calmly breathed to avoid swallowing. Their cervical spines were in neutral position. Their heads and necks were in the middle of the HDNV Array head and neck coil, and their hands were on both sides of the body. Scanning range was from C1 to C7 level. The scanning parameters were as follows: field strength 40 mT/m, switching rate 150 mT/m/s. FSE sequence sagittal T1 WI (TE26.1 ms, TR2927 ms), T2 WI (TE117.6 ms, TR3200 ms), axial T2 WI (TE120.2 ms, TR2500 ms), and DTI (TE87.2 ms, TR8000 ms) scans were performed on all subjects, with slice thickness of 3 mm, sagittal field of view (FOV) 240 mm × 240 mm, and axial FOV 180 mm × 180 mm. DTI used a single stimulated echo planar imaging (EPI) sequence, with a b value (Dispersion Sensitive Gradient, DSG) of 1000 s/mm², FOV 24 mm × 24 mm, slice thickness 4 mm, slice spacing 0.4 mm, and scanning matrix 130 × 128.

All scanning images were conveyed to the Advantage Workstation Volume Share 5 (GE Medical Systems S.C.S, France). DTI data image processing is performed using GE Functool 9.4.05 software. The correct programme was used to correct the scanned images. Then DTI images, apparent diffusion coefficient (ADC) colormaps and fractional anisotropy (FA) colormaps of the corresponding cross-sections of the cervical spinal cord were obtained. Normal subjects were analysed according to the regions of interest (ROI)

(C2–C3, C3–C4, C4–C5, C5–C6 and C6–C7 level corresponding to spinal cord), which was determined by the FSE T2 WI sequence. The patients with CSM were examined by MRI pre-operatively, 1 week, and 1, 3 and 6 months post-operatively. The ROI was selected according to the FSE T2 WI sequence, including C2–C3 (white arrow), C3–C4 (blue arrow), C4–C5 (red arrow), C5–C6 (green arrow) and C6–C7 (yellow arrow) intervertebral disc level corresponding to the cervical spinal cord. Additionally, the level of T2 hyperintensity or maximum compression level (MCL) on T2 WI was recorded. The DTI parameters of all ROIs were measured and recorded: ADC values and FA values. Corresponding DTI images, ADC and FA colormaps of the spinal cord in patients with CSM are shown in Fig. 2. Scales of ADC colormaps and FA colormaps are shown in Fig. 3. To reduce subjective errors, all measurements were done by a spine surgeon and a radiologist, respectively. The final results were determined as the average of the two.

Statistical analysis

All data were described as the mean ± standard deviation (SD), and all statistical analyses were performed using the statistical software SPSS 19 (IBM SPSS Statistics, USA). Differences of DTI parameters between maximum compression level of spinal cord in CSM patients and the same level in normal subjects were tested for statistical significance using two-sample *t* tests. Pearson's correlation analysis was used to investigate relationships between the FA value at the maximal compression level of the spinal cord in CSM patients and the mJOA score and Nurick grade. *P* < 0.05 was considered statistically significant.

Results

1. There were significant differences in DTI parameters of the spinal cord between normal subjects and patients with CSM (ADC: 1.119 ± 0.087 vs. 1.395 ± 0.091 , *P* < 0.01; FA: 0.661 ± 0.057 vs. 0.420 ± 0.080 , *P* < 0.01). The ADC value of the spinal cord increased, but the FA value decreased at the maximal compression level of the spinal cord in patients with CSM (Table 2).
2. DTI images, ADC colormaps and FA colormaps corresponding to the C2–C3 (white arrow), C3–C4 (blue arrow), C4–C5 (red arrow), C5–C6 (green arrow) and C6–C7 (yellow arrow) intervertebral level of the cervical spinal cord are shown in Fig. 2. The DTI images, ADC colormaps and FA colormaps of the cervical spinal cord in patients with CSM not only reflected compression of the spinal cord from the form but also reflected the functional status of the spinal cord from the visual colour changes. In ADC colormaps, the ADC value increased

Table 1 mJOA score and Nurick grade (mean ± SD) of patients with CSM at different times (*n* = 60)

Time	mJOA score	Nurick grade
Pre-operation	10.61 ± 2.32	3.47 ± 0.71
Post-operation 1 week	13.02 ± 2.43	3.01 ± 0.62
Post-operation 1 month	14.17 ± 2.13	2.63 ± 0.48
Post-operation 3 months	15.36 ± 1.98	2.31 ± 0.51
Post-operation 6 months	15.43 ± 2.01	2.29 ± 0.50

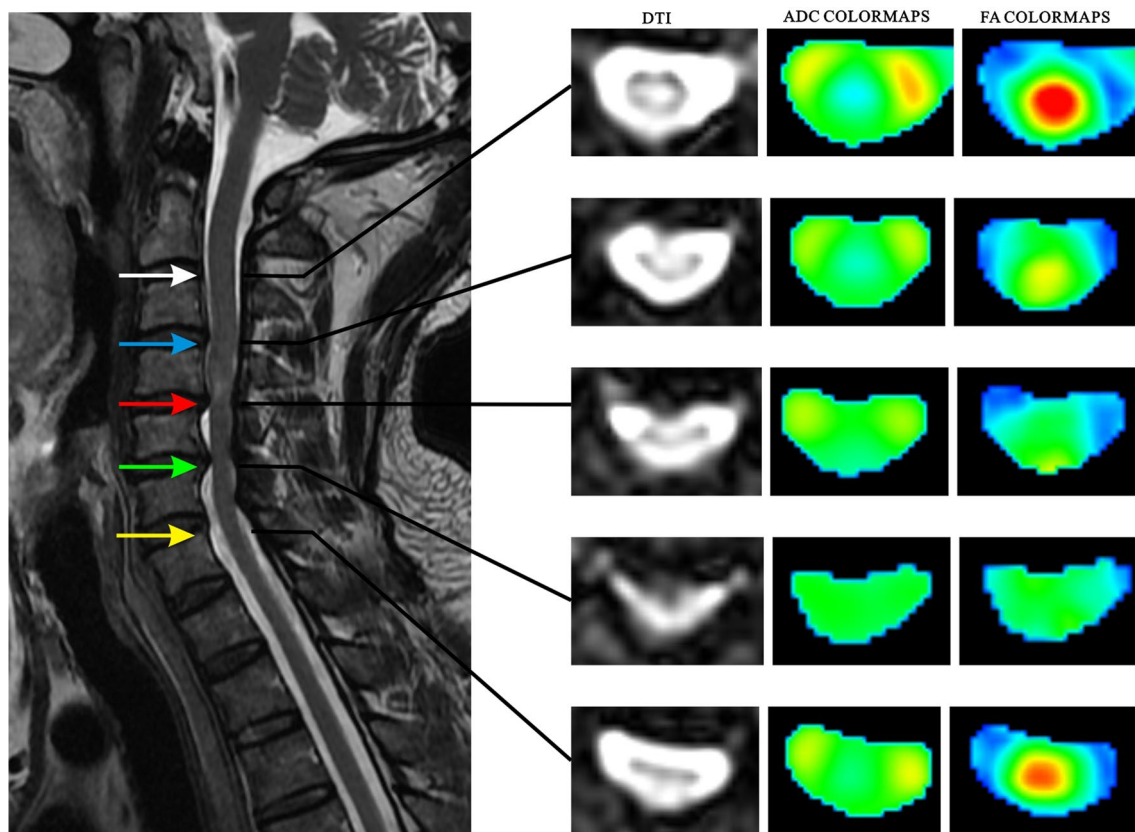


Fig. 2 DTI images, ADC colormaps and FA colormaps corresponding to the C2–C3 (white arrow), C3–C4 (blue arrow), C4–C5 (red arrow), C5–C6 (green arrow) and C6–C7 (yellow arrow) intervertebral level of the cervical spinal cord in patients with CSM

as the spinal cord compression increased, which was manifested as a colour change from blue to → green. However, in the FA colormaps, the FA value gradually reduced as the spinal cord compression increased, which was manifested as a colour change from red to → yellow to → green (Fig. 2).

3. The FA values at the maximal compression level of the spinal cord in patients with CSM were significantly associated with the mJOA score pre-operatively, 1 week, and 1, 3 and 6 months post-operatively, with Pearson's coefficient correlations of 0.58 ($P < 0.01$), 0.53 ($P < 0.05$), and 0.51 ($P < 0.05$), 0.54 ($P < 0.05$) and 0.55 ($P < 0.05$), respectively (Table 3). However, they were negatively and significantly associated with the Nurick grade, with Pearson's coefficient correlations of -0.40 ($P < 0.05$), -0.39 ($P < 0.05$), and -0.41 ($P < 0.05$), -0.45 ($P < 0.05$) and -0.44 ($P < 0.05$), respectively (Table 4).

Discussion

With the ageing of the world population, the incidence of CSM has increased each year, especially in young patients. This seriously jeopardises people's health. Thus, early diagnosis and treatment is urgently necessary. In the existing CSM imaging diagnostic technology, MRI undoubtedly plays a crucial role.

The shortcomings of traditional MRI

MRI provides excellent anatomical images of the macroscopic structure of the spinal cord, clearly showing compression and signal changes of the spinal cord, and even showing some pathological changes. Histopathological changes in CSM include myelomalacia, oedema gliosis

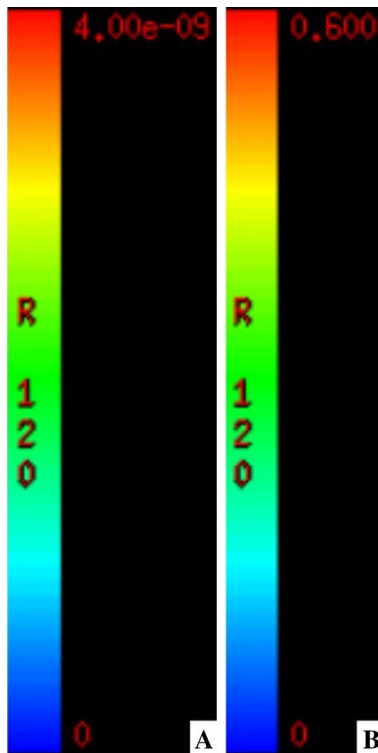


Fig. 3 Scale of the ADC colormaps and FA colormaps. **a** ADC; **b** FA

Table 2 ADC and FA value between the maximal compression level of patients with CSM and the same level of normal subjects (mean ± SD)

	Normal	CSM	<i>P</i>
ADC ($\times 10^{-3}$ mm ² /s)	1.119 ± 0.087	1.395 ± 0.091	< 0.01
FA	0.661 ± 0.057	0.420 ± 0.080	< 0.01

Table 3 Correlations between the FA value of the maximal compression level and mJOA score in patients with CSM at different times

mJOA score	Pearson’s correlation coefficient	<i>P</i>
Pre-operation	0.58	< 0.01
Post-operation 1 week	0.53	< 0.05
Post-operation 1 month	0.51	< 0.05
Post-operation 3 months	0.54	< 0.05
Post-operation 6 months	0.55	< 0.05

and ischaemic changes in white matter, which are the pathological basis of the high signal in the spinal cord on MR T2 WI [1, 16]. Some scholars believe that these changes indicate irreversible damage of the spinal cord [3]. Therefore, if a patient’s traditional MR T2 WI shows a high signal, this indicates the function of the spinal cord

Table 4 Correlations between the FA value of the maximal compression level and Nurick grade in patients with CSM at different times

Nurick grade	Pearson’s correlation coefficient	<i>P</i>
Pre-operation	− 0.40	< 0.05
Post-operation 1 week	− 0.39	< 0.05
Post-operation 1 month	− 0.41	< 0.05
Post-operation 3 months	− 0.45	< 0.05
Post-operation 6 months	− 0.44	< 0.05

has been severely damaged; thus, surgery is often slightly too late.

Many of the current radiological anatomical images are often inconsistent with the functional status of the patient, placing clinical treatment in a dilemma [17]. For example, the same MR images may have different clinical manifestations in different people. This makes clinical diagnosis and timely treatment of CSM challenging, urging for a new MRI technique.

DTI in CSM

DTI can quantify the size and direction of water molecules diffusion in tissues, which reflects the integrity of axon fibres in the spinal cord and small pathological changes of the spinal cord [18, 19]. The FA value is the most commonly used quantitative description of the dispersion of the diffusion tensor index [20]. ADC is the mean of the diffusion rate, and its increase or decrease depends on the process of histopathological damage of the tissue. The 3.0-T MR can provide higher image quality in DTI of the cervical spinal cord and better accordance with the expected anatomy compared to 1.5-T. In general, DTI parameters are affected by microstructural changes in tissues that affect the diffusion of water molecules, which is difficult to detect by traditional MRI. This is the theoretical basis of DTI in the diagnosis and evaluation of post-operative spinal cord function in patients with CSM.

It is interesting that in our study, in patients with CSM, the ADC value is elevated and FA value decreased, which is in contrast to acute compression of spinal cord [21, 22]. The changes in patients with CSM are very similar to those observed in chronic spinal cord injury [23, 24] and are also confirmed by animal models of chronic spinal compression. We conclude that this may be due to chronic, recurrent ischaemic damage of the spinal cord leading to downstream nerve fibre histopathology changes, including gliosis, neuron function loss, angioedema and eventual necrosis and cavitation. These pathological changes are intertwined, leading to an increase in the ADC value at the site of the spinal cord compression (increase of extracellular water) and decrease

of the FA value (reduced anisotropy tissue). In the ADC colormaps and FA colormaps of patients with CSM, we can clearly visualise the above changes in DTI parameters (Fig. 2).

A study completed by Jones et al. [25] showed that patients with a high pre-operative FA value were likely to achieve better functional recovery after surgery. We analysed the FA values of spinal cord in 60 patients with CSM, compared it with the mJOA score and Nurick grade at different times, and found the FA value was positively correlated with the mJOA score but negatively correlated with the Nurick grade. Therefore, we believe that the FA value at the site of the spinal cord compression can be used as a potential imaging marker in selecting appropriate surgical cases, or that it can serve as a useful predictor of surgical outcomes.

Studies have found that a high pre-operative MR T2 WI signal indicates poorer neurological outcomes following surgery, and it may continue to exist even if patients' mJOA score and Nurick grade are constantly improving [26]. Compared with an all-or-none high signal on T2 WI, the FA value is a continuous variable, which can provide a more accurate description of the spinal function in patients with CSM. Moreover, under the clinical suspicion of cervical myelopathy, DTI can find the abnormal microstructure changes of the spinal cord before a high signal emerges on traditional MR T2 WI. Although DTI was able to identify and quantify the severity of the spinal cord injury, we suggest that the establishment of the clinical FA value for the prognosis of spinal cord recovery still requires a larger sample size and multicentre, randomized controlled prospective studies.

In conclusion, DTI colormaps of spinal cord in patients with CSM can reflect compression and functional status of spinal cord. The FA value of spinal cord was associated with post-operative recovery of spinal cord function. These suggest DTI may play a significant role in diagnosing and predicting the development of CSM.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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