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The role of diffusion tensor imaging in the early detection and prognosis of cervical spondylotic myelopathy

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Abstract

Background: Cervical spondylotic myelopathy (CSM) is a spinal disorder stemming from cervical spine degeneration, elevating the potential for spinal cord damage. Diffusion tensor imaging (DTI) represents an advanced MRI technique utilized to detect subtle alterations in the spinal cord induced by CSM. This paper aims to examine the function and prognostic significance of DTI in the early identification of CSM.

Aims and Objectives: The principal goals and objectives of this research are outlined as follows: 1. The significance of diffusion tensor imaging in assessing initial changes in the spinal cord that T2A-MRI fails to reveal; 2. A comparison of DTI (diffusion tensor imaging) metrics (FA and ADC) with clinical symptoms (mNURICK s and mJOA scores); 3. The forecasting ability of DTI regarding postoperative outcomes in degenerative cervical spondylosis.

Materials and Methods: In our investigation, we scrutinized 30 hospitalized individuals at our university-associated healthcare facility, who exhibited mild myelopathic symptoms but showed no T2-weighted MRI indicators. They were diagnosed with degenerative compressive cervical myelopathy based on DTI imaging. Patients were slated for surgical procedures via either an anterior or posterior method, with or without the incorporation of fusion or fixation apparatus. Each patient underwent DTI imaging both prior to and following the surgery. The post-operative DTI assessment analyzed fractional anisotropy (FA) and apparent diffusion coefficient (ADC). The modified Japanese Orthopaedic Association (mJOA) evaluation was administered before and after the surgery. A regression formula was developed.

Results: Our analysis revealed that the FA value at the compression stage is considerably reduced compared to the non-compression stage ($p=0.005$), while the ADC value at the compression stage is elevated relative to the non-compression stage ($p<0.001$). This validates the actual level of compression observed. Following the DTI analysis, the assessment of compression degree showed remarkably enhanced results (FA value increased $p < 0.001$, ADC value decreased $p < 0.001$). Additionally, the postoperative enhancements in FA and ADC values exhibited a significant correlation with the improved mJOA scores. Nevertheless, the predictive strength for the FA value stands at 71.8%, while that for the ADC value is 45.5%. The anticipated improvement in the postoperative score surpasses the actual score; however, the statistical relevance of this observation could not be confirmed due to the limited number of subjects.

Conclusion: DTI has demonstrated its efficacy as a remarkable instrument for the timely identification of CSM and the forecasting of outcomes and potential complications in individuals affected by CSM.

Keywords: Diffusion tensor imaging (DTI), Cervical spondylotic myelopathy (CSM), Fractional anisotropy (FA), Apparent diffusion coefficient (ADC), Modified japanese orthopedic association (mJOA).

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1. Introduction

The primary reason behind issues in the cervical spine is cervical spondylotic myelopathy (CSM), a condition that progressively deteriorates over time.[1,2] This may involve either direct compression of the spinal cord or pressure on adjacent nerves. Research indicates that spondylosis is the leading factor for cervical spondylosis in individuals aged 50 and above.[3] It is estimated that 100,000 people are hospitalized each year for CSM, and the number of patients requiring surgical treatment is increasing sevenfold each year.[4,5] The nature and impact of mental disorders vary, making optimal management difficult. Spinal cord ischemia and micro-injuries represent two significant aspects of spinal cord damage within the framework of CSM. Even following decompressive surgery, distinctive magnetic resonance imaging (MRI) characteristics of CSM, such as heightened spinal cord signal intensity observed on T2-weighted scans,

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frequently manifest later in the progression of the illness. To achieve optimal outcomes, it is essential to recognize and address CSM promptly, prior to the onset of spinal cord injury.[6,7]

The intricate pathophysiology of CSM inherently leads to compensatory mechanisms within the spinal cord. Anatomically, the spine is under pressure from disc protrusions, vertebral deformities, enlarged facet joints, bone spurs, thickened ligament flavum, and ossified posterior longitudinal ligament. This degenerative cascade results in consistent compression of the spinal cord and may induce additional compression during movement. Ultimately, both static and dynamic pressures can lead to venous congestion, ischemia of the spinal cord caused by vascular pressure, and injuries from axonal tension.[8] Given that magnetic resonance imaging (MRI) is insufficient in identifying minor early alterations in the spinal cord, there is a need for a novel neuroimaging method that can reveal early spinal cord damage prior to the appearance of T2 hyperintensity.[9,10] DTI represents an advanced MRI method that is adept at identifying variations among water molecules within tissue cells and the surrounding extracellular compartments. This capability permits the formulation of a metric known as the diffusion tensor (DT), which characterizes the macroscopic organization of white matter at a voxel scale of several millimeters. Consequently, diffusion tensor imaging (DTI) emerges as a pivotal magnetic resonance imaging approach that aids in the prompt detection of cervical spondylotic myelopathy (CSM). Evidence suggests that early intervention through decompression surgery yields superior outcomes compared to delayed procedures. The current investigation has been conducted to examine the significance of DTI in monitoring initial alterations in the myelon and its prospective prognostic implications post-surgery for patients diagnosed with degenerative cervical myelopathy

2. Materials and Methods

A collective group of 30 individuals exhibited cervical discomfort and radicular pain in the outpatient department of SMS Medical College, participating in the research from March 2022 to March 2023. Commonly observed clinical symptoms and signs were recorded. The Modified Nurick grading scale and the mJOA score were acquired. Diffusion tensor (DT) imaging and DTI parametes (FA and ADC) were captured from both stenotic and nonstenotic regions of the patients. Patients with other neurological conditions, those in need of repeat surgeries, or who developed infections at surgical sites were excluded. Based on clinical indications, the patients underwent surgical decompression utilizing either an anterior or posterior method, with or without the fixation of titanium implants.(**Table 1**)

All patients had pre-operative 3.0-Tesla MRI and DTI of the cervical spine after receiving institutional ethics committee approval (**Figure 1**). Following full wound healing and the edemain the soft tissues subsided, postoperative DTI imaging was performed two weeks following the procedure.

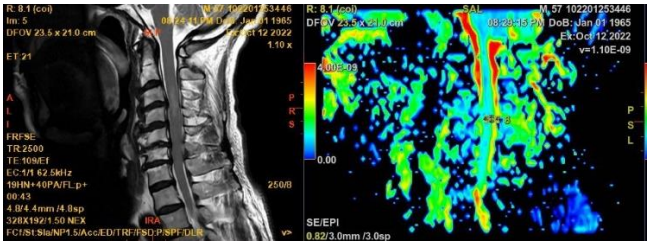

Figure 1: T2WI MRI and DTI-scan of cervical spine

Table 1: Factors that would promote one approach over another

Sagittal alignment	**Kyphosis**	**Fixed – anterior** **Flexible- anterior or posterior with fusion**
	Neutral or lordotic	Posterior (laminoplasty)> anterior
No of level	>3	Posterior (laminoplasty)> anterior
	<2	Anterior > posterior
Age and Comorbidities	Elderly, greater comorbidities	Posterior > anterior
	Healthier	Anterior > posterior
Re-opeartive pain levels	Moderate- high	Anterior or posterior with fusion
	None-low	Posterior (laminoplasty)> anterior
Instability	Yes	Anterior or posterior with fusion
	No	Posterior (laminoplasty)

Table 2: Modified Nurick (mNurick) grading for cervical myelopathy

Grade 0	No root or cord symptoms
Grade 1	Signs or symptoms of root involvement only – no spinal cord symptoms
Grade 2	Signs of spinal cord involvement ; normal gait
Grade 3	Mild gait abnormality : doesn't prevent employment
Grade 4	Gait abnormality prevents employment
Grade 5	Only able to walk with assistance
Grade 6	Chair bound or bedridden

Table 3: Modification of mJOA score (mJOA score)

Modified Japanese Orthopaedic Association (mJOA) score	
I. Motor dysfunction score of the upper extremities	Circle one
Not able to move hands	0
Not able to eat with a spoon but able to move hands	1
Not able to button shirt but able to eat with a spoon	2
Able to button shirt with great difficulty	3
Able to button shirt with slight difficulty	4
No dysfunction	5
II. Motor dysfunction score of the lower extremities	Circle one
Complete loss of motor and sensory function	0
Sensory preservation without ability to move legs	1
Able to move legs but unable to walk	2
Able to walk on flat floor with a walking aid (i.e., cane or crutch)	3
Able to walk up and/or down stairs with hand rail	4
Moderate to significant lack of stability but able to walk up and/or down stairs without hand rail	5
Mild lack of stability but walk unaided with smooth reciprocation	6
No dysfunction	7
III. Sensation	Circle one
Complete loss of hand sensation	0
Severe sensory loss or pain	1
Mild sensory loss	2
No sensory loss	3
IV. Sphincter dysfunction	Circle one
Not able to urinate voluntarily	0
Marked difficulty with micturition	1
Mild to moderate difficulty with micturition	2
Normal micturition	3
Mild myelopathy	mJOA from 15 to 17
Moderate myelopathy	mJOA from 12 to 14
Severe myelopathy	mJOA from 0 to 11.

Table 4: Comparison of FA value at C-level between pre-operative and post-operativeperiods

Parameters			**N**	**Mean**	**SD**	**t- value**	**P-value**
Pre-OPMean FA- NC Level	Age	<50 years	12	0.52	0.06	1.504	0.144
		>50 years	18	0.47	0.1		
	Sex	Male	22	0.48	0.09	0.435	0.667
		Female	8	0.5	0.07		
	m-nurickGrade	2	6	0.51	0.07		
		3	21	0.48	0.09		
		4	3	0.51	0.07	0.542	0.588
Pre-OPMEAN FA- C Level	Age	<50 years	12	0.44	0.07	0.728	0.472
		>50 years	18	0.41	0.11		
	Sex	Male	22	0.41	0.09	0.815	0.422
		Female	8	0.44	0.09		
	m-nurickGrade	2	6	0.45	0.07		
		3	21	0.41	0.1		
		4	3	0.44	0.1	0.574	0.570
Post-OP FA –C Level	Age	<50 years	12	0.5	0.08	1.327	0.195
		>50 years	18	0.45	0.1		
	Sex	Male	22	0.46	0.09	0.63	0.534
		Female	8	0.49	0.1		
		2	6	0.5	0.07		
	m-nurick Grade	3	21	0.47	0.1	0.325	0.725
		4	3	0.44	0.08		

Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) are seen in both preoperative and postoperative images. Demographic information such as age, gender, as well as preoperative and postoperative modified nurick levels (**Table 2**) and modified Japanese Orthopaedic Association (mJOA) (**Table 3**) scores were also calculated.

2.1. Statistical analysis

Data organization and examination were performed utilizing Microsoft Excel and SPSS version 20 software, respectively. Categorical variables were displayed using frequency and percentage. Continuous variables were represented as mean and standard deviation, and comparisons were made using independent t-tests, paired t-tests, and one-way ANOVA. Logistic regression was employed for multivariate analysis. The significance threshold was maintained at $p<0.05$.

3. Results

The majority of study participants (40.0%) were <50 years old, 73% were male. Comparison of the FA and ADC values between <50 years and > 50 years, betweenmales and females and between mNurick grades (2, 3 and 4) did not reveal any significant difference in both compression and non-compression levels. (**Table 4**, **Table 5**)

The mJOA score also did not significantly vary between <50 years and > 50 years, between males and females but it was significantly decreased with the increase in the mNurick grades.(**Table 6**)

Mean mJOA score in preoperative period was 13.06±1.63 and in post-operative period 14.83±1.31. Recovery rate was calculated using hirabyashi method (**Table 7**).

Hirabayashi method: Recovery rate recovery rate (%) = (postoperative JOA score − preoperative JOA score) × 100/(17 −preoperative JOA score)

Clinical results were divided into four groups as followed: 75% or higher (excellent) ,50% -74% (good), 25%– 49 % (fair), and less then 25% (poor).

Mean mJOA recovery ratio in our study as 44.92±38.57. Mean mJOA recovery rate in grade II nurick change group is 48.12±27.68 and in grade III group is 46.72±64.32. So overall we found recovery rate in our study population is in fair group.

The relative strengths of FA and ADC values were 71.8% and 42.5%, respectively. Only 71.8% of the time could the postoperative mJOA score be correctlypredicted using the preoperative FA values, according to this statistic. (**Table 8**) It wasalso discovered that in severe instances (mJOA =9), the projected postoperative improved score is higher than the actual.

Table 5: Comparison of ADC value between pre-operative and post-operativeperiods

Parameters			N	Mean	SD	t- value	P- value
Pre-OP Mean ADC- NCLevel	Age	<50 years	12	1.47	0.17		
		>50 years	18	1.5	0.14	0.379	0.707
	Sex	Male	22	1.48	0.14		
		Female	8	1.52	0.17	0.613	0.545
	m-nurick Grade	2	6	1.52	0.14		
		3	21	1.49	0.16		
		4	3	1.41	0.16	0.468	0.631
Pre-OP Mean ADC-CLevel	Age	<50 years	12	1.88	0.15		
		>50 years	18	1.89	0.2	0.232	0.818
	Sex	Male	22	1.89	0.17		
		Female	8	1.88	0.19	0.152	0.880
	m-nurick Grade	2	6	1.92	0.05		
		3	21	1.88	0.2		
		4	3	1.9	0.19	0.133	0.876
Post OPADC -C Level	Age	<50 years	12	1.58	0.13		
		>50 years	18	1.65	0.1	1.439	0.161
	Sex	Male	22	1.62	0.13		
		Female	8	1.63	0.07	0.151	0.879
	m-nurick Grade	2	6	1.62	0.08		
		3	21	1.61	0.13		
		4	3	1.68	0.05	0.413	0.666

Table 6: Comparison of mJOA scores between pre-operative and post-operative periods

Parameters			N	Mean	SD	t- value	P-value
Pre-OP mJOA ScoreS	Age	<50 years	12	12.75	1.6	0.831	0.413
		>50 years	18	12.22	1.77		
	Sex	Male	22	12.59	1.65	0.84	0.408
		Female	8	12	1.85		
	Nurick Grade	2	6	10.33	0.82	22.861	0.003
		3	21	12.62	1.16		
		4	3	15.33	0.58		
Post-OP mJOA Scores	Age	<50 years	12	15.25	1.14	0.291	0.773
		>50 years	18	15.11	1.37		
	Sex	Male	22	15.27	1.16	0.758	0.455
		Female	8	14.88	1.55		
	Nurick Grade	2	6	13.83	1.17	6.966	0.004
		3	21	15.38	1.07		
		4	3	16.33	0.58		

Table 7: Correlation of mJOA recovery ratio with demographic and radiological findings

Parameter		mJOA recovery ratio	P- value	t- value
Age	< 50 years	67.24± 45.78	0.157	1.68
	>50 years	43.08±36.01	0.157	1.68
Grade II MRI finding		48.12±27.68	0.542	1.45
Grade III MRI findings		46.72±64.32	0.384	1.12
Pre-op FA value	<0.4	38.43±12.52	0.0164	1.89
	>0.4	54.72±34.12	0.0164	1.89

Table 8: Regression models and formula for different variables at postoperative period (mJOA as dependent variable)

Variables	Unstandardized Coefficients		Standardized Coefficients	t	P value	95% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	14.345	1.274		11.261	0.000	11.736	16.955
FA at C level	1.036	2.653	0.074	0.391	0.699	-4.399	6.471
(Constant)	10.339	3.359		3.078	0.005	3.458	17.220
ADC at C level	2.772	2.067	0.246	1.341	0.191	-1.461	7.005
(Constant)	10.246	3.474		2.949	0.007	3.118	17.373
FA at C level	0.406	2.672	0.718	0.152	0.880	-5.076	5.889
ADC at C level	2.711	2.141	0.455	1.266	0.216	-1.682	7.104
Variables				**Regression formula**			
For mJOA and FA				mJOA = 14.345 + 1.036 (FA)			
For mJOA and ADC				mJOA = 10.339 + 2.772 (ADC)			
For mJOA and FA, ADC				mJOA = 10.246 + 0.406 (FA) + 2.711 (ADC)			

Table 9: Comparison of the results with similar recent studies.

Author (Year)	Mean FA values		Mean ADC values (x 10^{-3} mm^2/s)	
	Non stenotic	Stenotic	Non stenotic	Stenotic
Toktas ZO et al.[33] (2015)	0.6884 ± 0.0075	0.4228 ± 0.1090	0.9183 ± 0.1477	1.312 ± 0.2405
Nukala M et al.[34] (2018)	0.729	0.48	0.90	1.25
Hassan T et al.[35] (2019)	0.742	Significantly reduced	-	-
Our study	0.480	0.420	1.48	1.88

4. Discussion

In the current senior demographic, degenerative compressive cervical myelopathy represents a prevalent spinal cord injury globally. This medical field encompasses a range of infectious and congenital disorders, such as degenerative disc illness, ossification of the posterior longitudinal ligament, and thickening of the ligamentum flavum, along with cervical spine conditions that may or may not involve instability in the region.[12-15] Static or dynamic x-rays, CT, myelography, or conventional MRI are frequently used to diagnose CSM. The effectiveness of conventional imaging techniques in diagnosing and predicting early response to treatment is still debatable despite the substantial advancements in conventional MRI technology since the field's start. The most wildly used method for assessing the morphological alterations in cervical spondylosis and spinal cord dysfunction is conventional MRI. Ischemia in the spinal cord and inflammation caused by microtrauma leading to apoptosis of neurons and oligodendrocytes are the primary mechanisms underlying spinal cord injury in patients with CSM. These pathological changes signify spinal cord edema or alterations in glial cells and typically manifest as elevated signals on T2-weighted images.[16] As the disease progresses, there is a noticeable increase in T2-weighted signal alterations observed in the cervical spine. Hori M et al. noted that there is only a positive association between clinical symptoms and MR imaging results.[17]

A relatively new MRI method called diffusion tensor imaging (DTI) captures earlier and better these microstructural alterations in white matter fibers than traditional MR imaging. Conventional MRI operates on the principle of isotropic diffusion, where water molecules move uniformly in all directions, using ADC values to reflect the average extent of molecular displacement and measure isotropic diffusion. In contrast, DTI capitalizes on anisotropic diffusion parameters that illustrate the organized movement of water molecules along a definitive path (parallel bundles of myelinated axonal fibers).[18] This is particularly observed in white matter, where alterations in the direction and volume of water diffusion are identified. Anisotropic diffusion is quantified by the FA value, with a score of 1.0 denoting anisotropic diffusion and a score of 0 indicating isotropic diffusion. FA value evaluates the directionality of molecule displacement through diffusion.[19] Compared to standard MRI, DTI is sensitive to disease processes that alter the microstructural behavior of water molecules in the cervical spine.[20] Compared to conventional MRI, DTI has better sensitivity for early diagnosis of spinal cord diseases.[21,22]

Similar pathological changes in tissue microstructure caused by spinal cord stimulation can be detected using DTI. For example, based on previous studies, the present findings showed that FA decreased and ADC increased at a higher frequency than usual in patients with cervical spine compression.[23,24] FA decreased and ADC increased compared to the level of neurological impairment determined by the mJOA score. Our findings support other researchers' observations that FA and ADC measurements at the region of compressionare potent indicators of identifying those with symptomatic stenosis.

In our study, the mean FA value of the stenotic segment (0.420) was lower than that of the non-stenotic segment (0.480). There was a significant difference in the mean ADC values between the stenotic segment (1.48) and the non-stenotic segment (1.88). Similar results were found in previous studies as described in (**Table 9**).

Our study found that these levels were improved with decompression surgery. mJOA was used in the pre- and post-treatment evaluation of these patients. As a result of statistical analysis, a positive correlation was found between preoperative FA and ADC values and postoperative mJOA scores.

Mean mJOA recovery ratio in our study as 44.92±38.57. Mean mJOA recovery rate ingrade II nurick change group is 48.12±27.68 and in grade III group is 46.72±64.32. So overall we found recovery rate in our study population is in fair group.

While a prior investigation by Dousset et al.[25] identified DTI as being more effective than T2-weighted imaging in individuals with CSM, the initial documentation on the application of DT in CSM sufferers was authored by Demir et al. Song et al.[26] compared DTI with traditional MR imaging in 53 CSM patients and 20 healthy controls, revealing significant signal intensity alterations in T2-weighted images within the cervical cord in only 24 instances, while no irregularities were noted in the remaining 26 subjects (three cases were omitted from the analysis due to subpar MR image quality). Conversely, DTI imaging revealed abnormalities in the cervical spine in 39 instances: diminished signal intensity in FA, elevated ADC signal intensity, yellow light spots visible among color DTI images, and a normally colored blue spinal cord. Consequently, they deduced that color DTI is capable of detecting a greater number of lesions than conventional MRI, exhibiting higher ADC values and lower FA values in CSM patients compared to healthy individuals. In a separate study by Kara et al.[27] a total of 16 subjects presented with neurological symptoms alongside CSM manifestations, yet without spinal cord hyperintensity on T2-weighted imaging. Imaging at 3-T was conducted, with observed reductions in stenosis levels and increases in ADC measurements within spinal FA.

Our results align with the previously mentioned studies. According to our research, we observed that our patients exhibited no significant spinal alterations during standard T2W MRI assessments. Nevertheless, we discovered that the average FA (0.420) of the stenotic segment registered lower than that of the non-stenotic segment (average 0.480) and the average ADC (1.88 × 10-3 mm2/s) during the DTI scan. The

stenotic segment indicated a higher measurement compared to the non-stenotic segment (1.48 × 10-3 mm2/s), as illustrated below. This corroborates that DTI scans are progressively more effective for assessing early changes in CSM patients.

In the postoperative evaluation, we found that the FA value at the compression level increased (from 0.42±0.08 to 0.47±0.09) compared to the preoperative values ($p<0.001$), while the ADC decreased significantly (1.88 ± 0.08) $0.17 \sim 1.62 \pm 0.11$) ($p < 0.001$). We can conclude that DTI scans are useful for determining appropriate compression levels based on significant changes in DTI parameters. DTI scans are best at diagnosing early cord changes. Early spinal changes in patients after compression level surgery can be predicted and measured using these DTI parameters and mJOA correction level.

Nonetheless, our research presents several constraints. Firstly, our participant group was limited in size and there was no long-term follow-up of the patients. Furthermore, if a significant number of the patients eventually exhibited hyperintensity on T2-weighted scans during the follow-up, the suggested link between FA and the initial phase of CSM could merely be established. Nevertheless, all patients underwent surgical procedures, and many of these individuals required instrumentation for cervical stability, which hindered a DTI evaluation of the cervical spinal cord for them. A similar limitation has also been noted previously by Kara et al.[27] Consequently, it is impossible to estimate the percentage of our patients who may have shown T2 hyperintensity if not treated.

5. Conclusion

To sum up, this research underscores the vital importance of diffusion tensor imaging (DTI) in the prompt identification and forecast of degenerative cervical spondylotic myelopathy (CSM). The results emphasize DTI's capability to identify initial alterations in the spinal cord, anticipate outcomes after surgery, and relate to clinical evaluation scores, offering essential insights for the care of CSM patients.

6. Source of Funding

None.

7. Conflict of Interest

None.

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