Original article

Correlation of diffusion tensor imaging with clinical and neurological findings in patients with cervical spondylotic myelopathy

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ABSTRACT:

Background: Cervical spondylosis is a common degenerative disease of spine generally seen in old age, frequently causing compression of spinal cord and /or nerve roots by protruding disc or osteophytes. Magnetic Resonance Imaging (MRI) is the modality of choice for evaluation of patients with features of cervical spondylotic myelopathy. In addition to routine MRI sequences, advanced MR techniques like diffusion tensor imaging (DTI) can be used to obtain specific information about the spinal cord.

Materials and methods: It is a prospective observational study conducted in 30 patients who presented with clinical and neurological features of cervical spondylotic myelopathy, who had undergone MRI.

Result: All the patients had undergone routine MRI along with diffusion tensor imaging. The Apparent Diffusion Coefficient (ADC) and Fractional Anisotropy (FA) values of the spinal cord were measured at the level of normal spinal canal dimension and at the level where there is narrowing of the spinal canal. The ADC values were found to be high and the FA values were low at the level of the spinal canal stenosis in comparison with values measured at the level of normal spinal canal dimension, which were statistically significant.

Conclusion: DTI parameters showed significant correlation with the clinical parameters, suggesting that DTI can be used to detect microscopic changes related to compressive myelopathy, before changes are apparent in the routine MR sequences. This can enable us to intervene early to avoid irreversible damage to the spinal cord.

Key words: Cervical spondylotic myelopathy, Diffusion tensor imaging, Fractional anisotropy.

Introduction

Cervical spondylosis is a common degenerative disease of spine generally seen in old age, frequently causing compression of spinal cord and /or nerve roots by various pathological entities like protruding disc, osteophytes and thickening of ligamentous structures around the spinal cord.[1] Spondylotic myelopathy refers to compression of the spinal cord by the above mentioned structures leading to impairment of spinal cord function.[2] Cervical spondylotic myelopathy (CSM) is usually seen after the 5th decade. Patients with CSM usually present with symptoms of numbness and weakness in limbs, pain over shoulder and neck, incoordination. Magnetic Resonance Imaging (MRI) of cervical spine is non-invasive and accurate imaging tool in assessing the structural changes of spinal cord due to its high contrast and soft tissue resolution[3]. It helps to ascertain the site and the

severity of degenerative compressive myelopathy. It is also useful to exclude any other pathology, like neoplasm which can cause compressive myelopathy and mimic degenerative disc disease.

Classical MRI finding seen in compressive myelopathy is focal T2 hyperintensity in spinal cord at the level of a compressive lesion. This signal change is suggestive of either spinal cord oedema in acute cases, or gliosis and myelomalacia in chronic cases[4,5]. Oedema is associated with swelling of the spinal cord and chronic changes on the other hand show thinning of the spinal cord. Other imaging modalities like Computed Tomography (CT) and radiography play a complementary role in the evaluation of CSM. Due to its inherent high spatial resolution CT is better than MRI in the assessment of cortical bone, osteophytes and other calcified ligamentous structures. These structures can also cause spinal canal compromise. Plain radiography is still being used as an initial tool for evaluating degenerative disc changes[6]. The ultimate aim of doing imaging studies is to identify the spinal cord abnormalities early and take remedial measures to prevent further damage[7].

Aims:

1. To compare Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC) values of the spinal cord obtained at the level with above and below the level of spinal canal stenosis.
2. To compare the Diffusion Tensor Imaging (DTI) parameters with Nurick score and neurological examination findings.
3. To detect the early microscopic level structural abnormalities of spinal cord using DTI before overt, irreversible changes manifest in routine MR sequences.

Materials and methods:

It is a prospective observational study performed in 30 patients who were referred by the department of neurology. These patients presented with clinical symptoms and neurological findings suggestive of cervical myelopathy. The study period was from January 2018 to March 2019 at the department of Radiology and imaging sciences PSG Institute of Medical Sciences & Research. Prior to commencement of the study, clearance has been obtained from Institutional Human Ethical Committee and informed written consent has been taken from the participants. Patients with clinical and neurological features of CSM were included in the study. Patients with following abnormalities were excluded from the study: 1.focal or diffuse signal abnormality in the spinal cord. 2. History of cervical spine injury / surgery. 3. Focal lesions in the brain which may be the underlying pathology causing the neurological abnormality.

Prior to undergoing MRI all these patients were assessed symptom wise for the severity of CSM using Nurick score and neurological examination was performed to assess the power of lower and upper limbs. In Nurick score patients were categorized from grade 0 to 3, based on clinical history alone, where grade 0 represented mild form of disease with only symptoms suggestive of nerve root involvement (radiculopathy), grade 3 represents more severe neurological deficit where the patients are wheel chair bound with no independent mobility (myelopathy). On clinical examination muscle power of the limbs was assessed using standard grade 1 to grade 5.

All the patients underwent MRI in Siemens 1.5 Tesla 16 channel machine.

MRI protocol:

1. Routine non contrast T1 and T2 weighted images to look for overt signal changes in T2 Weighted Images.
2. DTI acquisition using EPI yielding the following set of images:

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1. Diffusion weighted imaging, 2.Trace weighted, 3.FA and ADC mapping 4.Tensor imaging.

DTI parameters:

Diffusion directions measured – 20.

The b factors – 0, 100 and 1000

TR/ TE - 3600 /94ms

Field of view - 230mm

Slice thickness - 5mm.

Images were analysed using Siemens Syngo via work station. Initially presence of any focal or diffuse spinal cord lesions was excluded. After that dimension of the spinal canal was measured at all the vertebral level. Subsequently DTI analysis was performed by drawing region of interest at the level of maximum spinal canal stenosis, one vertebral level above the spinal canal stenosis and one level below (Figure 1a). DTI Parameters assessed were FA and ADC, the values of which were displayed as a table in the system (Figure 1b) along with images of visual maps of ADC (Figure 2a) and FA (Figure 2b).

Statistical analysis:

The data has been analysed using SPSS 23.0 version. To describe the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & standard deviation (SD) were used for continuous variables. To find the significant difference in the multivariate analysis for repeated measures the repeated measures of ANOVA was used with Bonferroni correction to control the type I error on multiple comparison. To assess the relationship between the variables Pearson's Correlation was used. In all the above statistical tools the probability value .05 is considered as statistically significant.

Results:

A total of 30 patients were enrolled in our study of which 20 were men and 10 were women (Figure 3). Nurick Score distribution is given in the table 1.

All the patients had muscle power grade between III and V. (Figure 4). No patient in our study had muscle power less than 3.

Diffusion tensor parameters (ADC and FA) were measured at 3 levels of the spinal cord (Figure 1a). One measurement at the level of the spinal canal stenosis and 2 measurements (above and below the level of stenosis) at the level of normal canal dimension. The values of ADC and FA measured at different levels of the spinal cord are given in table 2.

Pairwise comparison of ADC and FA was performed and results are given in table 3 and table 4. Patients were found to have high ADC and low FA values at the level of stenosis when compared with ADC and FA values at the level of no stenosis. The differences were found to be statistically highly significant with a p value of 0.0005 (ANOVA test was used). There was negative correlation between the mean FA and ADC at the level of stenosis with r value of -0.424 and p value of 0.019. There was negative correlation between the mean FA and ADC at the level of no stenosis with r value of -0.0545 and p value of 0.002. There is negative correlation between Nurick score (clinical grading) and muscle power (neurological examination) r value of -0.07 and P value of 0.001.

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Correlation of FA and ADC with muscle power:

At the level of stenosis:

There was a positive correlation between muscle power and mean FA value with r value of 0.2 and p value 0.1. There is a negative correlation between muscle power and mean ADC value at the level of stenosis with r value of -0.1 and p value 0.1 and p value of 0.3.

At the level of no stenosis:

There is a positive correlation between muscle power grade and mean FA value at the non- stenosis level with r value of 0.18 and p value 0.32 and p value of 0.4. There is a negative correlation between muscle power grade and mean ADC value at the non-stenosis level upper with r value of -0.25 and p value 0.17.

Correlation of FA and ADC with Nurick score:

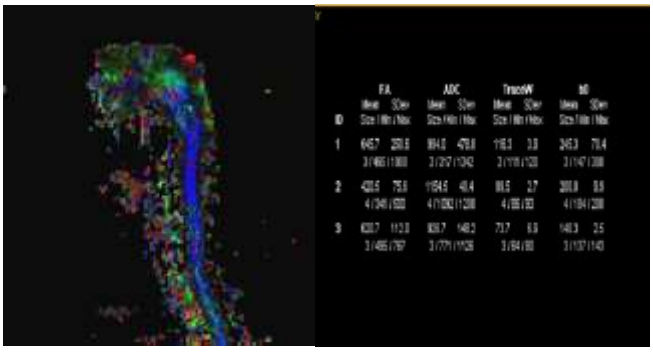
At the level of stenosis:

FA and Nurick score has negative correlation with r value of -0.4 and p value of .0005. ADC and Nurick score has a positive correlation with r value of -0.1 and p value of – 0.2

At the level of no stenosis:

FA and Nurick score had positive correlation with r value of 0.1 and p value of –0.4. ADC and Nurick score had negative correlation r value of -0.05 and p value of– 0.7

ROC analysis of FA in predicting microscopic level structural cord abnormality in the spinal cord at the level of the spinal canal stenosis. (Figure 5) was done. Subsequently test result variables (table 5) and sensitivity and specificity (table 6) were calculated. Likewise ROC analysis of ADC in predicting microscopic level structural cord abnormality was done (Figure 6). Test result variables (table 7) and sensitivity and specificity (table 8) were also calculated for ADC. Both FA and ADC showed good sensitivity and specificity in predicting the early microscopic level changes in the spinal cord caused by degenerative disease, ADC was slightly more specific than FA.



a **b**

Figure 1. Method of FA and ADC measurement.

Three circular Region of Interest (ROI) are drawn “at”, “above” and “below” the level of stenosis (a) yielding the numeric values of each level in a table (b).

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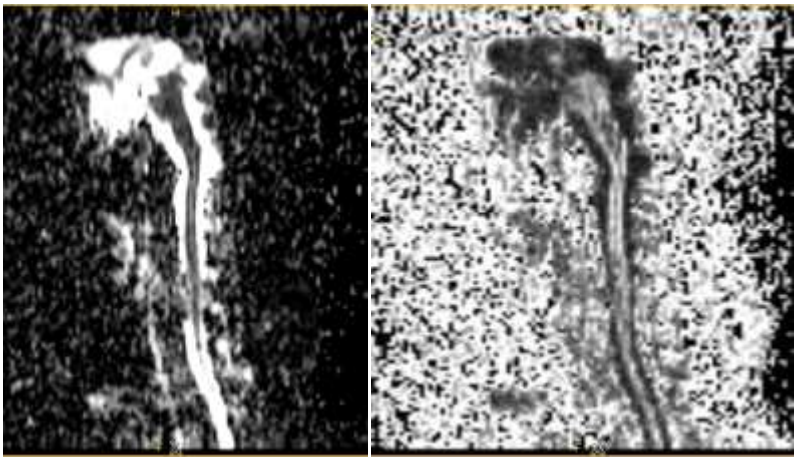

a b

Figure 2. ADC (a) and FA (b) maps obtained with DTI.

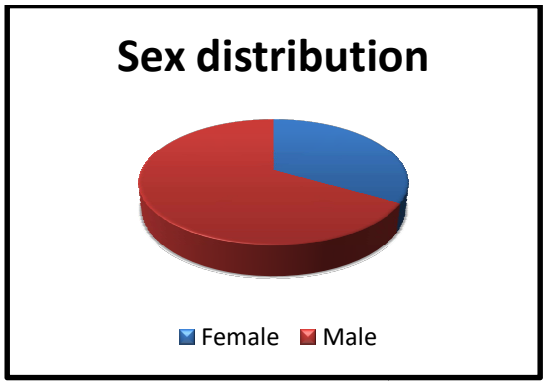

Figure 3. Sex distribution in the study population.

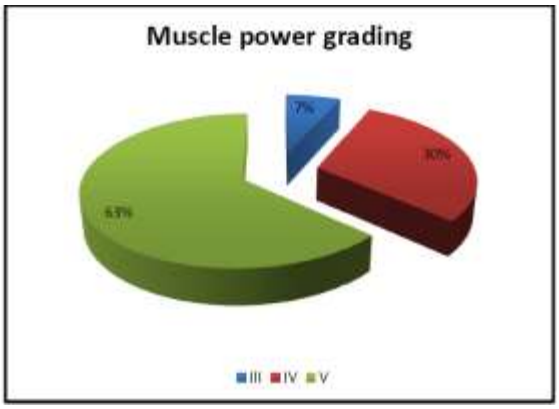

Figure 4. Muscle power distribution in the study population.

Majority of the patients had a muscle power of 5. Remaining patients had muscle power of 4 and 3.

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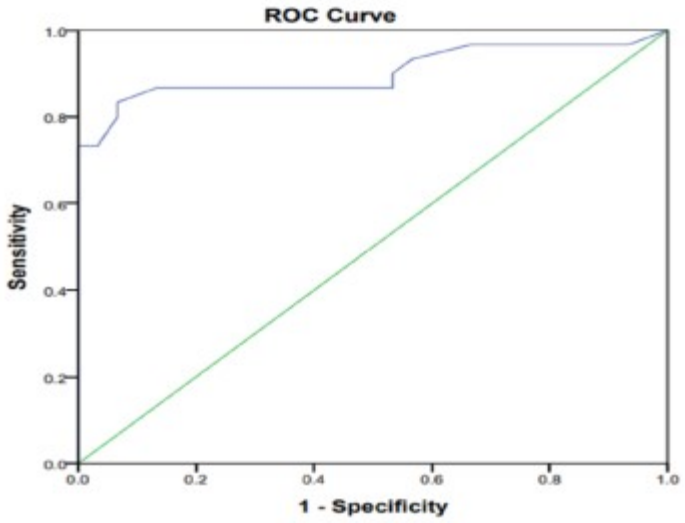

Figure 5: ROC analysis of FA in predicting the microscopic structural abnormality in the spinal cord.

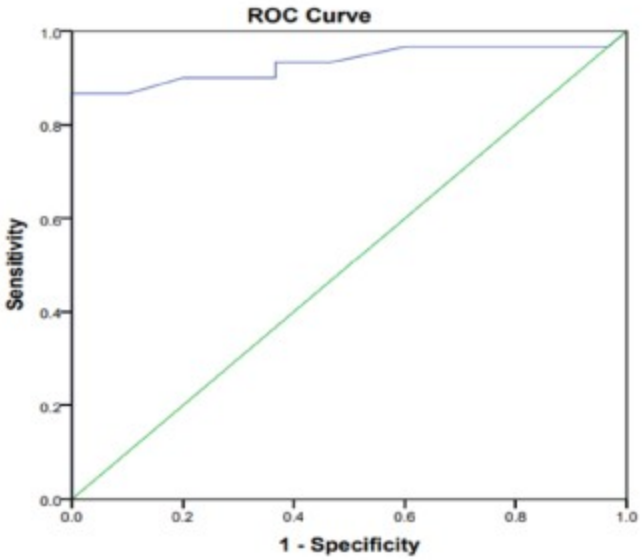

Figure 6: ROC analysis of ADC in predicting the microscopic structural abnormality in the spinal cord.

Table1: Nurick Score distribution in the study population:

Nurick Score	Number	Percent
0	2	6.7
1	9	30.0
2	9	30.0
3	10	33.3
Total	30	100.0

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Table 2: Values of ADC and FA measured at different levels of the spinal cord.

	ADC		FA	
Level of spinal cord	Mean	SD	Mean	SD
Stenotic Level	1.3470	.23997	.5067	.09484
Non-stenotic level upper	1.0141	.09272	.6670	.07957
Non-stenotic level lower	1.0120	.08919	.63443	.07566

Table 3: Pairwise comparison of ADC

(I) ADC		Mean Difference (I-J)	Std. Error	Sig.[b]
Mean ADC stenotic level	Mean ADC non-stenotic level upper	.333*	.045	.0005
	Mean ADC non-stenotic level lower	.335*	.043	.0005
Mean ADC non-stenotic level upper	Mean ADC stenotic level	-.333*	.045	.000
	Mean ADC non-stenotic level lower	.002	.021	1.000
Mean ADC non-stenotic level lower	Mean ADC stenotic level	-.335*	.043	.000
	Mean ADC non-stenotic level upper	-.002	.021	1.000

Based on estimated marginal means.

*The mean difference is significant at the .05 level.

b. Adjustments for multiple comparisons: Bonferroni.

Table 4: Pairwise comparison of FA:

(I) FA		Mean Difference (I-J)	Std. Error	Sig.[b]
Mean FA stenotic level	Mean FA non-stenotic level upper	.160*	.019	.0005
	Mean FA non-stenotic level lower	.128*	.023	.0005
Mean FA non-stenotic level upper	Mean FA stenotic level	-.160*	.019	.000
	Mean FA non-stenotic level lower	.033	.017	.219
Mean FA non-stenotic level lower	Mean FA stenotic level	-.128*	.023	.000
	Mean FA non-stenotic level upper	-.033	.017	.219

Based on estimated marginal means.

*The mean difference is significant at the .05 level.

b. Adjustments for multiple comparisons: Bonferroni.

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Table 5: Test result variables of FA

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.902	.045	.0005	.815	.990

Table 6: Sensitivity and specificity calculation of FA.

Predictor	Cut off	AUROC	Sensitivity	Specificity
FA	0.57	0.902	86.7%	86.7%

Table 7: Test result variables of ADC.

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.932	.039	.0005	.857	1.000

Table 8: Sensitivity and specificity calculation of ADC.

Predictor	Cut off	AUROC	Sensitivity	Specificity
ADC	1.1	0.932	86.7%	90.0%

Discussion:

MRI has revolutionized the evaluation of pathology related to spinal cord. Exceptionally high contrast resolution and soft tissue resolution place MRI way above other imaging modalities in the evaluation of spinal cord.[2] Recent advances in respect to high field strength and fast and robust sequences have greatly contributed to the superior performance of MRI[8]. Very small yet important structures like the nerve roots and the thin ligaments need to be assessed in almost all patients which can harbour the pathology. However significant degree of anatomical and structures abnormalities need to be present before they are visible in routine MRI sequences, primarily in the spinal cord[6]. Hence the need for imaging technique which is similar to a biomarker to pick up early microscopic level changes in the neural structures, specially the spinal cord. Role of DTI in the evaluation of the brain pathologies has been proved and it is being used routinely, however its usage in the evaluation of spinal cord is still evolving.

The application of DTI in the evaluation of spinal cord is hindered by various factors. Spinal cord is a very narrow structure with a high elasticity and situated in anatomically complex location, which are the factors

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making evaluation difficult. Other factors like CSF pulsation, motion artefacts and breathing related artefacts make usage of DTI difficult as a routine sequence. Newer techniques like reduced field of view with oblique spin echo and OVS (outer volume suppression) have been used to overcome the limitations and better images can be obtained. All these improved techniques provide high resolution images not only in the cervical cord but also the entire spinal cord.

Budzik et al[9] studied the feasibility of DTI and fiber tracking in CSM. FA values showed correlation with the patients' clinical scores. High signal intensity of the spinal cord on T2WI did not correlated either with the DTI parameters or with the clinical symptoms, suggesting that FA is better in depicting the early structural abnormality of the spinal cord when compared with T2W imaging[10, 11]. But they did not study the relationship of DTI scalars with cervical canal width. In our study all the patients had spinal canal stenosis, in that about 73% of the patients had relative narrowing and 27% has absolute narrowing.

In our study degenerative changes like disc bulge, protrusion, osteophytes and ligament thickening led to spinal canal narrowing. These pathological changes caused disruption of the white matter tracts and other secondary changes in cervical cord. Secondary changes like cord edema and macrophage proliferation lead to increased diffusivity of water molecules with in the spinal cord parenchyma, especially in the white matter which can alter the FA and ADC values[12]. These changes were apparent much before macroscopic changes appear in routine T1 and T2W images.**UzeyirAhmadli et al**[13] investigated the utility of DTI sequence in patients with CSM symptoms for early detection of microscopic changes in the spinal cord at the level of narrowed spinal canal without any T2 signal alterations. FA values with in the cord were reduced and ADC increased at site of canal stenosis when compared with non-stenotic segments above the level of canal stenosis. However no significant difference was noted in FA and ADC values between stenotic segment and non-stenotic segment distal to the level of stenosis.

In our study there was statistically significant reduction in the FA values and increase in the ADC values at the site of stenosis when compared to the non-stenotic levels (upper and lower). There was no statistically significant reduction in FA value noted at the non-stenotic levels (upper and lower). The reduction in FA value at the stenotic level is presumably due to reduced neuronal fibers with increase in the extracellular space or due to extracellular edema which can result in increased diffusivity of water molecules and consequently facilitated diffusion.

Jones et al[14] reported a significant correlation between FA and modified Japanese orthopedic association score and Nurick score, and reported that patients who had a higher FA at the compressed level of spinal cord tended to have a better recovery of functionality after surgery when compared to patients undergoing surgery who had a lower FA value pre operatively. In our study there was significant correlation between the patient’s symptoms and the DTI parameters. We graded clinical symptoms using only Nurick score, modified Japanese orthopedic association score was not used.

FA and Nurick score had a negative correlation with r value of -0.4 and p value –0.0005, which implies that the FA values tend to be less when the Nurick score is on the higher side. ADC and Nurick score had a positive correlation with r value of-0.1 and p value of – 0.2, which is equal to higher ADC means higher Nurick score.There was also a significant correlation between the DTI parameters and muscle power. There was positive correlation between muscle power and mean FA value at the level of stenosis with r value of 0.2 and p

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value of 0.1. There is a negative correlation between muscle power and mean ADC value at the level of stenosis with r value of -0.1 and p value of 0.3. ROC was calculated between the stenotic and non stenotic level. The mean was calculated between the upper and lower non-stenotic level and it was compared with the stenotic level. FA showed a sensitivity of 86.7% and specificity was 86.7% when the cut was kept at 0.57 (Table 6). ADC showed a sensitivity of 86.7% and specificity was 90.0%, when the cut off is kept at 1.1. (Table 8).

Conclusion:

- Our study showed significant correlation between the patients' clinical symptoms and DTI parameters.
- DTI has the potential to detect microscopic structural changes in the spinal cord, before the T2 signal changes appear on conventional MRI.
- DTI can be used as a tool for detecting early changes in cervical spondylotic myelopathy, which would prognosticate the clinical and surgical outcome[14, 15].
- DTI technique should be routinely used on patients with clinical symptoms of cervical spondylotic myelopathy.

Limitations:

- The sample size of the study population was relatively small
- The long-term follow-up of the patients were not done
- It was impossible to determine the percentage of patients with early cervical spondylotic myelopathy who would have advanced to T2 hyperintensity changes in spinal cord, when left untreated.
- Cost and the availability of MRI.

Further studies have to be done on large group with long term follow up of those patients to determine the potential utility of quantitative diffusion tensor imaging.

Conflicts of interest:

There are no conflicts of interest to declare.

Acknowledgments:

Dr.Arun, Assistant professor, Dept of community medicine for his immense help in demystifying statistics used in the study.

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