



Efficacy of diffusion tensor imaging in identification of degenerative cervical spondylotic myelopathy

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ABSTRACT

Aim and objectives: To study the diagnostic accuracy of Diffusion tensor imaging technique in detection of cervical spondylotic myelopathy changes.

Material and method: Study population included 50 patients with symptoms of cervical myelopathy. The patients were evaluated based on symptoms using the European myelopathy scoring system and were divided into: Grade 1, including patients with mild symptoms; Grade 2, referring to patients with moderate symptoms and Grade 3, which included patients revealing severe symptoms. All the patients were investigated with a 1.5 T MRI unit acquiring DWI and DTI sequences. FA and ADC values from each spinal segment were analyzed in terms of Frequency, Percentage, Mean, Standard Deviation and Confidence Intervals. The comparison of values was done by ANOVA and post hoc analysis by bonferroni test. Comparison of accuracy of FA, ADC and T2WI in recognizing myelopathic changes was done by t-test. Receiver Operating Characteristics (ROC) analysis was performed to obtain a cut off value of FA and ADC for each spinal level to identify myelopathic change in the spinal cord.

Results: The study revealed a significant difference in the mean FA and ADC value of stenotic and Non-stenotic segments. T2WI was highly significant ($p = 0.000$) in recognizing myelopathy changes in patients falling under Grade 2(moderate) and Grade 3(severe) according to European Myelopathy scoring system. Regarding patients under Grade 1 (mild) FA and ADC values showed significant difference compared to T2WI. The collective sensitivity in the identification of myelopathic changes was highest with FA (79%) as compared to ADC (71%) and T2WI (50%). ROC analysis was done to determine the cut off values of FA and ADC at each cervical spine segments. The proposed cut off, for FA and ADC at the level of C1–C2 is 0.68 and 0.92, C2–C3 is 0.65 and 1.03, C3–C4 is 0.63 and 1.01, C4–C5 0.61 and 0.98, At C5–C6 0.57 and 1.04, At C6–C7 0.56 and 0.96 respectively. **Conclusion:** FA and ADC values enhance the efficacy and accuracy of MRI in the diagnosis of cervical spondylotic myelopathy. Hence diffusion tensor imaging can be used as a non-invasive modality to recognize spondylotic myelopathy changes even in the early stages, which can be helpful in deciding on appropriate timing of decompression surgery before the irreversible chronic changes set in.

1. Introduction

Degenerative cervical spine disorder is the most common non-traumatic disorder of the spine, found in more than 75% of individuals after the age of 65 years [1].

Cervical spondylotic myelopathy is monitored using clinical symptoms and imaging modalities, mainly plain radiography, and conventional magnetic resonance imaging. Although conventional MRI is the modality of choice for identification of spondylotic changes and secondary complication to the spinal cord, it is known to have a low

sensitivity for myelopathy changes, estimating to about 65% [1]. The high signal intensity in the cord on T2 weighted images appears in late clinical stages.

The changes of cord due to myelopathy on conventional MRI were divided into three stages according Ramanaukas et al. [2]. According to them the early stage that is due to edema; this is seen as increased signal intensity involving the width of the spinal cord. Intermediate stage is characterized by cystic necrosis of grey matter. Late stage is irreversible with a sharply delineated high signal within the cord on T2 weighted images and low signal on T1 weighted images representing

Abbreviations: DTI, diffusion tensor imaging; ADC, apparent diffusion coefficient; FA, fractional anisotropy; T2WI, T2 weighted imaging; ROC, receiver operating characteristics

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cystic necrosis, syrinx formation and atrophy.

Diffusion tensor imaging (DTI) is based on the diffusion rate of water in tissue. Diffusion anisotropy in white matter originates from its specific organization in bundles of myelinated axonal fibers running in parallel [3]. Disruption of axonal structure changes the anisotropic diffusion (Directionally dependent diffusion) to isotropic diffusion (Diffusion in all directions); this can be measured by apparent diffusion coefficient (ADC), which is the average magnitude of molecular displacement. A increase in this numeric value implies that the medium is isotropic. Fractional anisotropy (FA) is the directionality of molecular displacement by diffusion, which varies between 0 (isotropic) and 1 (infinite anisotropic diffusion).

Hence, DTI is sensitive to disease processes altering the water movement in cervical spinal cord at a microscopic level beyond the conventional MRI [4].

Conservative treatment options like bracing and traction are effective for mild myelopathic symptoms. However, if disease process is prolonged without improvement, then the opportunity for surgery would also be lost and have a poor post-operative outcome [5].

The purpose of the study was to evaluate the usefulness of DTI in recognition of patient with early stage changes of cervical spondylotic myelopathy, in order to emerge as a aid to conventional magnetic imaging in identifying patients reacquiring early management before the chronic irreversible changes ensue.

2. Material and methods

2.1. Study population

Fifty symptomatic patients (21 women and 29 men; age range 30–60 years) were enrolled in the study from July of 2015 to September of 2017. A written and informed consent was obtained from all the patients before MRI.

The inclusion criteria for the patients were clinical signs and symptoms of degenerative cervical spine disease; the patients were assessed based on European myelopathy scoring system, which Vitzthum et al. [6] concluded as the most appropriate scoring system to evaluate the clinical state and severity of CSM, the patients were categorized into grade 1 (mild), grade 2(moderate) and grade 3(severe) according to their symptoms.

Patients with congenital spinal canal narrowing, central spinal canal widening, and previous spinal surgery and with any incidental findings on plain MR images suggestive of neurological disorder that could bias the results (e.g. inflammatory changes) were excluded from the study.

The study was conducted in accordance with the guidelines of the University Ethics Committee for conducting research involving humans. Each patient provided his or her signed informed consent to participate in the examination.

2.2. MRI protocol

All examinations were performed using a 1.5 T scanner (MAGNETOM, SIEMENS).

Unenhanced T1 and T2 weighted sequences were performed before DTI in order to obtain a morphological evaluation of the spinal cord, recognize significant cord change as high signal on T2 weighted images and serve as a reference image to compare the sensitivity of DTI over T2 weighted image in identifying early changes.

Protocol Examination included:

- Diffusion – single shot echo planar imaging TR3200TE99Slice thickness3.0mmFOV300mAcquisition time3min 33 sSlice20-Average3Diffusion direction20Echo spacing0.85PlaneSagittalb-value800
- T1 weighted image:TR625TE11Slice thickness3.0mmFOV270m-Slice13Average2PlaneSagittal

- T2 weighted image:TR3200TE106Slice thickness3.0mm-FOV270mSlice13Average2PlaneSagittal
- T2 weighted image:TR8000TE1200Slice thickness50.0mm-FOV280mSlice1Average2PlaneCoronal

2.3. Image analysis

Plain MR images of the cervical spine of 50 patients were analyzed. Each spine segment from C1/C2 to C6/C7 was evaluated separately in terms of signs of degenerative spine disease and if there was presence of myelopathy changes on conventional T2 weighted images was noted.

The DTI images were analyzed with a post processing NEURO-3D software on GE. Apparent diffusion coefficient (ADC) and Fractional anisotropy (FA) transverse maps were generated. Region of interest were drawn manually with a pixel size of 4 on the reference T2 weighed image at each spinal segment level.

2.4. Statistical analysis

For each of these cases, the patient's age, gender, FA value at each spinal segment level, ADC value at each spinal segment level, Maximum compression level, conventional T2WI characteristics and EMS score were recorded. Data was collected in Microsoft Excel spreadsheet.

Collected Data was analyzed by frequency, percentage, mean, standard deviation and confidence intervals.

Comparison of FA and ADC values was done by ANOVA, KAPPA test and fisher's exact test. ROC (receiver operating characteristic) analysis was performed to obtain a cut off value for FA and ADC at different spinal segments.

3. Results

3.1. Qualitative analysis

Morphological analyses were done on T2 weighted images based on the presence and absence of high signal intensity on the affected region of the spinal cord. Some patients showed presence of altered signal intensity in these areas. On evaluation of tensor images some showed a change in the colour of the normal spinal cord on tensor image blue (cranio-caudal direction) to green(antero posterior direction) or red (medio-lateral direction). Out of the 50 patients 21 showed changes on T2 weighted images out of which 7 belonged to grade 2 and 14 belonged to grade 3 (Figs. 1–5).

3.2. Quantitative analysis

The patient's distribution into three grades, on the basis of symptoms was as follows (Table 1): 23 patients had grade 1 symptoms; 11 patients had grade 2 symptoms and 16 patients had grade 3 symptoms.

Comparing mean values of FA (Fig. 1), ADC (Fig. 2) between stenotic and non-stenotic segments of the cervical cord revealed that the average mean FA value in stenotic segment was 0.48 compared to 0.729 in non-stenotic segments and the average mean of ADC values in Stenotic segments was 1.25 compared to 0.9 in non- stenotic segments.

Tables 2–4 show that the P-value for T2 weighted imaging is $p = 0.000$, which implies high significance to recognize to show myelopathic changes in grade 3 but T2WI performed very poorly in recognizing myelopathy changes in grade 1 (0%), however FA and ADC performed better in recognizing myelopathic changes in grade 1 patients, about 31% and 26.9% respectively.

(Table 5) compares the sensitivity, specificity, positive predictive value and negative predictive value of FA, ADC and T2 weighted image, FA showing the highest sensitivity and specificity.

In recognition of myelopathic changes in cervical spinal cord, with FA values the ROC curve (Fig. 3) showed an area under the curve depicted in (Table 6) and cut off values (Table 7) proposed for each level

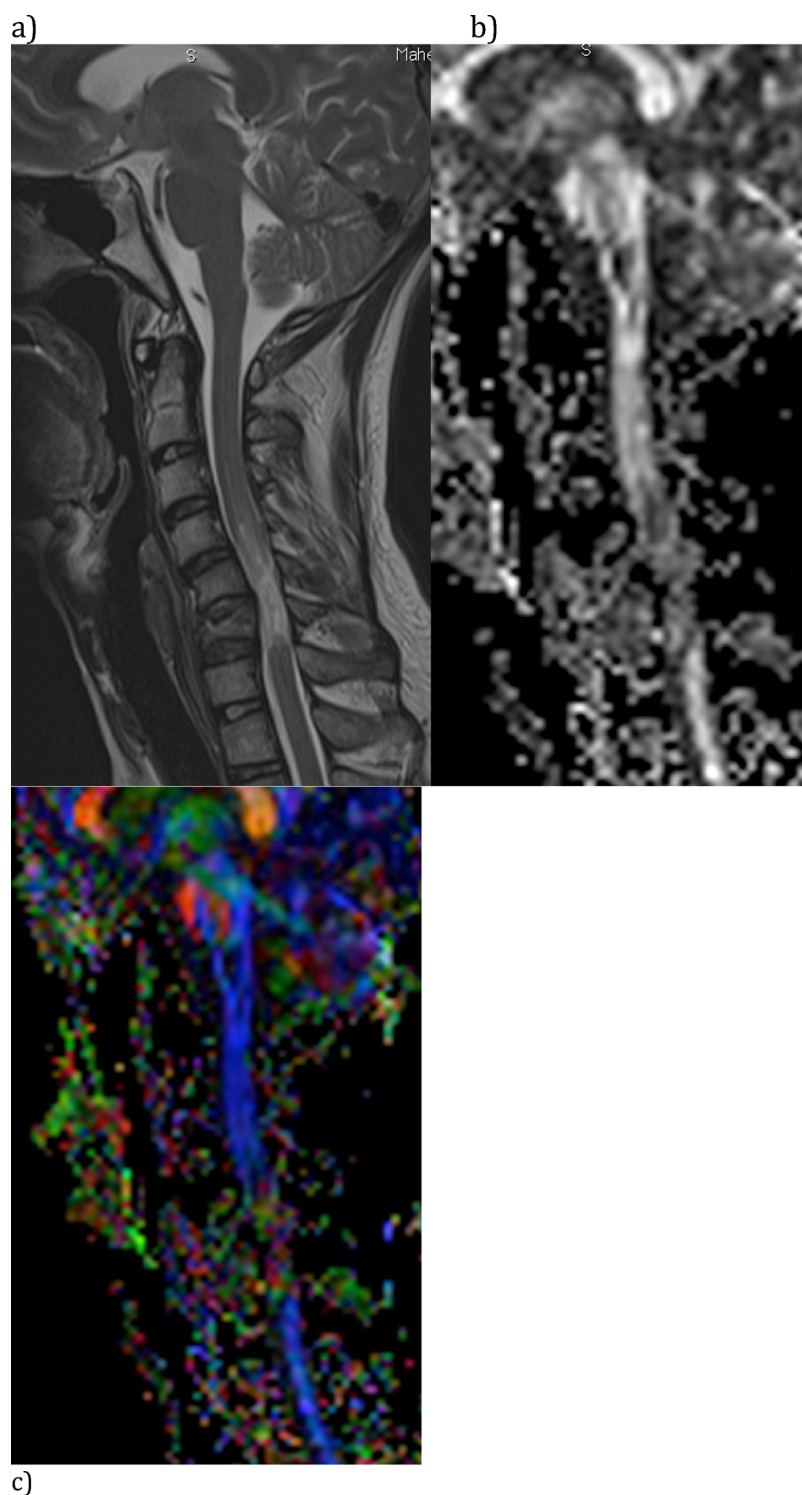


Fig. 1. 57 year old patient presented with symptoms correlating with EMS grade 3. a) T2 weighted images show increased signal intensity at C4–C6 level, This area shows b) reduced FA and ADC values and c) Tensor images shows loss of blue colour of the normal cord.

of cervical spinal segment.

In recognition of myelopathic changes in cervical spinal cord, with ADC values the ROC curve (Fig. 4) showed an area under the curve depicted in (Table 8) and cut off values (Table 9) proposed for each level of cervical spinal segment.

In the prediction of myelopathy changes in cervical spinal cord at the level of C1–C2, the ROC curve of FA value showed area under the curve of 0.522, a 95% confidence interval (CI) for the area = 0.360–0.684, with sensitivity of 57% and specificity of 48%. The ROC

curve of ADC value at C1–C2 level showed area under the curve of 0.603, a 95% confidence interval for the area = 0.439–0.768, with a sensitivity of 69% and specificity of 58%.

In the prediction of myelopathy changes in cervical spinal cord at the level of C2–C3, the ROC curve of FA value showed area under the curve of 0.605, a 95% confidence interval (CI) for the area = 0.442–0.768, with sensitivity of 57% and specificity of 48%. The ROC curve of ADC value at C2–C3 level showed area under the curve of 0.692, a 95% confidence interval for the area = 0.541–0.843, with a

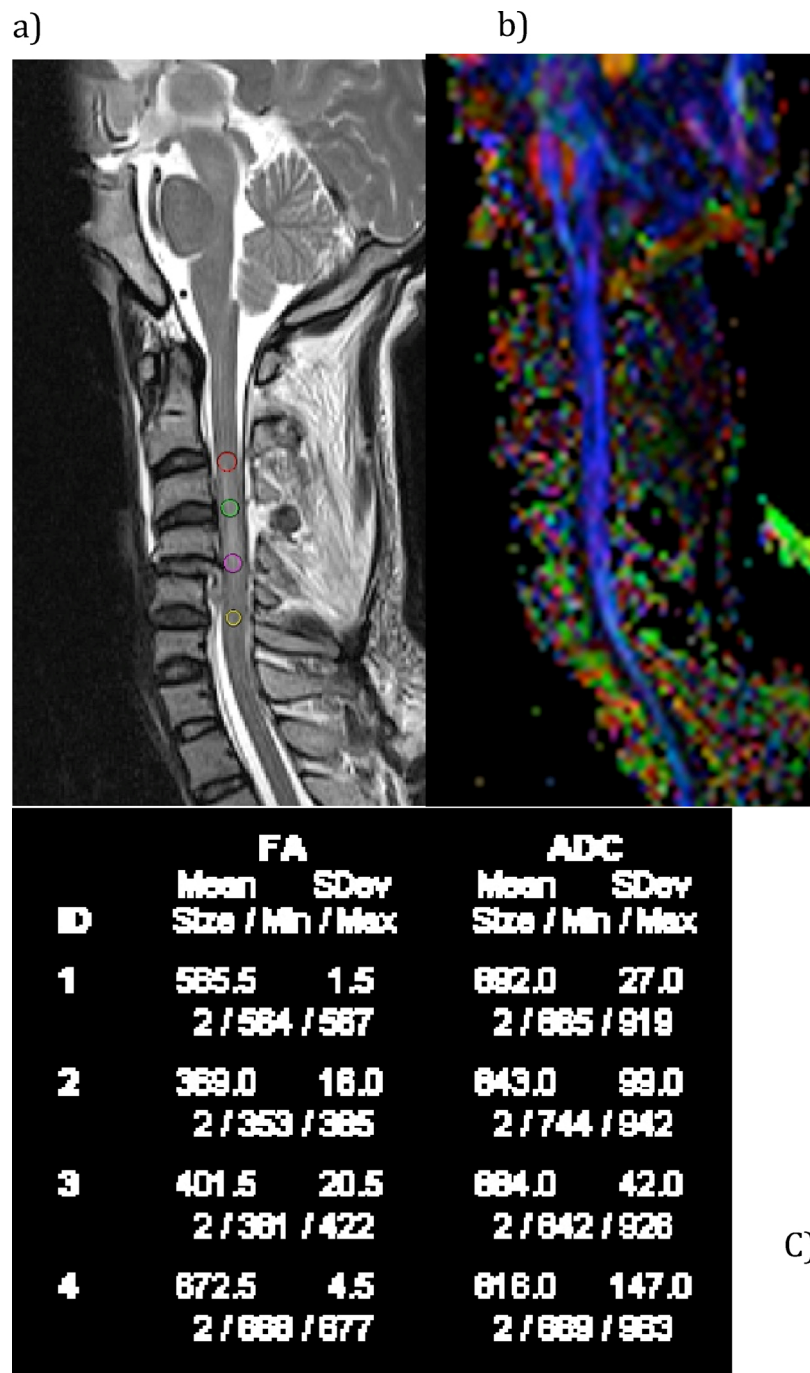


Fig. 2. 45-year-old male patient, presented with history of chronic neck pain belonging EMS grade 2. a) T2 weighted image shows disc protrusion indenting on spinal cord with altered signal in cord from C3–C5 spinal levels. B) Tensor maps don't show obvious change. There is a significant reduction of FA in C3–C4 and C4–C5 levels.

sensitivity of 65% and specificity of 37.5%.

In the prediction of myelopathy changes in cervical spinal cord at the level of C3–C4, the ROC curve of FA value showed area under the curve of 0.734, a 95% confidence interval (CI) for the area = 0.596–0.872, with sensitivity of 81% and specificity of 44%. The ROC curve of ADC value at C3–C4 level showed area under the curve of 0.915, a 95% confidence interval for the area = 0.837–0.993, with a sensitivity of 88% and specificity of 33.3%.

In the prediction of myelopathy changes in cervical spinal cord at the level of C4–C5, the ROC curve of FA value showed area under the curve of 0.792, a 95% confidence interval (CI) for the area = 0.669–0.916, with sensitivity of 85% and specificity of 34.5%. The

ROC curve of ADC value at C4–C5 level showed area under the curve of 0.841, a 95% confidence interval for the area = 0.734–0.949, with a sensitivity of 84% and specificity of 33.3%.

In the prediction of myelopathy changes in cervical spinal cord at the level of C5–C6, the ROC curve of FA value showed area under the curve of 0.859, a 95% confidence interval (CI) for the area = 0.754–0.963, with sensitivity of 85% and specificity of 27.6%. The ROC curve of ADC value at C5–C6 level showed area under the curve of 0.811, a 95% confidence interval for the area = 0.682–0.940, with a sensitivity of 80% and specificity of 33.3%.

In the prediction of myelopathy changes in cervical spinal cord at the level of C6–C7, the ROC curve of FA value showed area under the

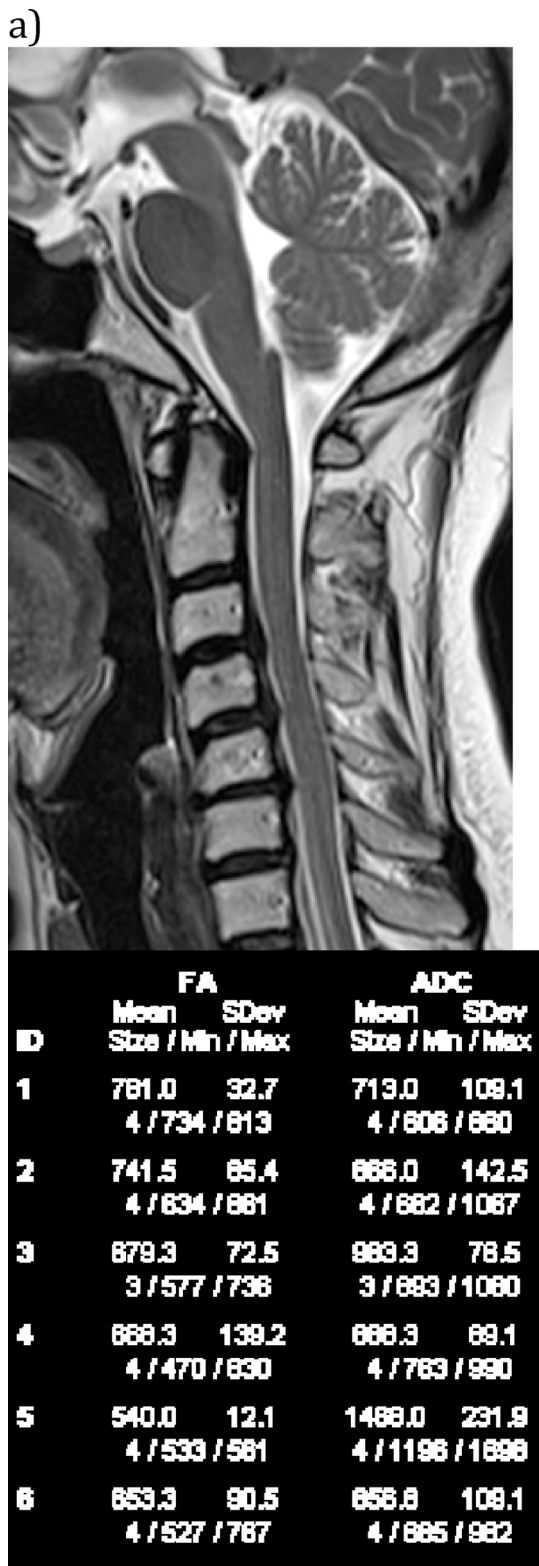


Fig. 3. 70 year old male presented with chronic neck pain with EMS grade of 2. a) T2WI shows no obvious changes, b) DTI shows a significant increase in ADC value (1.48) at C6–C7 level.

curve of 0.792, a 95% confidence interval (CI) for the area = 0.668–0.916, with sensitivity of 81% and specificity of 37.9%. The ROC curve of ADC value at C6–C7 level showed area under the curve of 0.768, a 95% confidence interval for the area = 0.627–0.908, with a sensitivity of 73% and specificity of 33.3%.

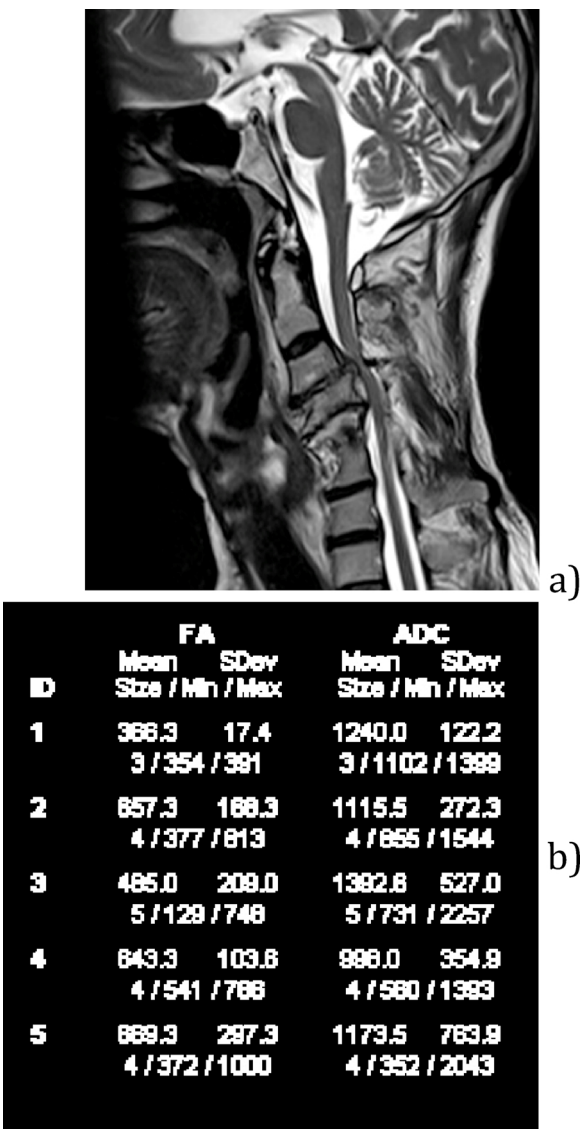


Fig. 4. 54 years old female patient presented with neck pain and EMS grade of 3. a) T2 weighted images showed severe canal stenosis and altered signal intensity within the cord. b) DTI metrics shows a decrease in FA and increase in ADC from C3–C5 level.

4. Discussion

MRI is the modality of choice for assessing cervical spondylosis [7]; however it has limited role in the evaluation of spinal cord involvement. Before the discovery of DTI the only way to assess the intrinsic cord structure was by T2WI and pathomorphological examination, now DTI has made it possible to evaluate the microstructure of spinal cord in vivo with a better sensitivity.

Demir et al. [1] were the ones who initially evaluated the use Apparent Diffusion Tensor (ADT) maps, Patients with myelopathy had abnormally increased ADC with a sensitivity of 80%, while T2 weighted images showed sensitivity of 61%.

Facon et al. [8] showed that in CSM patients with imaging evidence of compression who present with higher FA and lower ADC values are likely to have an acute compression having higher probability of recovery with surgery than patients with similar imaging feature but with low FA and high ADC values representing gliosis or myelomalacia.

Jones et al. [9] reported a strong correlation between FA and modified Japanese orthopedic association and nurick scores and also reported that patients who had a higher FA at the compressed level

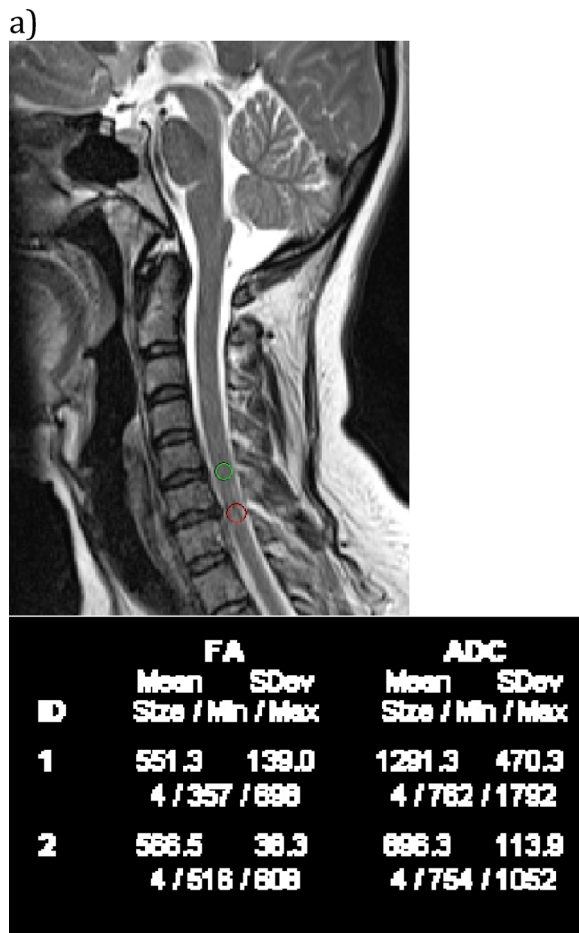


Fig. 5. 45 year old female patient presented with neck pain and EMS grade of 1. a) Showed no obvious altered signal intensity in spinal cord on T2 weighted image. However showed cervical spondylotic changes and disc bulge indenting on theca. b) DTI showed increase in ADC value at C6–C7 level, representing myelopathic change not apparent on conventional T2 weighted images.

Table 1
Distribution of European myelopathy score in patients studied.

	Frequency	Percent
Grade 1	23	46.0
Grade 2	11	22.0
Grade 3	16	32.0
Total	50	100.0

Table 2
Showing number of patients with FA representing positive or negative test compared to EMS (grade).

		EMS (Grade)			Total
		Grade 1	Grade 2	Grade 3	
FA	Positive	9	8	12	29
		31.0%	27.6%	41.4%	100%
		39.1%	72.7%	75.0%	58.0%
	Negative	14	3	4	21
		66.7%	14.3%	19.0%	100%
		60.9%	27.3%	25.0%	42.0%
Total		23	11	16	50
		46.0%	22.0%	32.0%	100.0%
		100.0%	100.0%	100.0%	100.0%

$X^2 = 6.239p = 0.044$, sig (Significant).

Table 3
Showing number of patients with ADC representing positive or negative test compared to EMS (grade).

		EMS (Grade)			Total
		Grade 1	Grade 2	Grade 3	
ADC	Positive	7	6	13	26
		26.9%	23.1%	50.0%	100%
		30.4%	54.5%	81.3%	52.0%
	Negative	16	5	3	24
		66.7%	20.8%	12.5%	100%
Total			45.5%	18.8%	48.0%
			23	11	16
			46.0%	22.0%	32.0%
			100.0%	100.0%	100.0%

$X^2 = 9.798p = 0.007$, HS (highly significant).

Table 4
Showing number of patients with T2 representing positive and negative test compared to EMS (grade).

		EMS (Grade)			Total
		Grade 1	Grade 2	Grade 3	
T2	Positive	0	7	14	21
		0%	33.3%	66.7%	100%
		0%	63.6%	87.5%	42.0%
	Negative	23	4	2	29
		79.3%	13.8%	6.9%	100%
100%		36.4%	12.5%	58.0%	
Total	23	11	16	50	
	46.0%	22.0%	32.0%	100.0%	
	100.0%	100.0%	100.0%	100.0%	

$X^2 = 32.367p = 0.000$, HS (highly significant).

Table 5
Comparison of sensitivity, specificity, positive predictive value and negative predictive value in FA, ADC and T2 weighted image.

	FA	ADC	T2
SENSITIVITY	78.8	71.4	50.4
SPECIFICITY	79.7	62.1	73.6
PPV	76.7	57.7	52.5
NPV	92.3	75.4	38.6

Table 6
Showing Area Under the Curve that is the most significant from C4–C7 levels with $p = 0.000$.

Test Result Variable (s)	Area	Std. Error	p	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
FA (C1–C2)	0.522	0.083	0.791	0.360	0.684
FA(C2–C3)	0.605	0.083	0.208	0.442	0.768
FA(C3–C4)	0.734	0.070	0.005	0.596	0.872
FA(C4–C5)	0.792	0.063	0.000	0.669	0.916
FA(C5–C6)	0.859	0.053	0.000	0.754	0.963
FA(C6–C7)	0.792	0.063	0.000	0.668	0.916

tended to have a better recovery of functionality after surgery when compared to patient undergoing surgery who had a lower FA value pre operatively.

Schalto et al. [10] in the MRI study of dynamic DTI of the cervical spine showed increase in ADC in the patient group in extension, in an attempt to identify early changes of myelopathy. Displacement of spinal cord in the spinal canal in dynamic motion, without spinal cord compression on Plain MR images may lead to abnormal patterns within the cord, which would decrease the FA. So DTI can show changes in cases

Table 7

Showing the cut off values of FA at each spinal cord level.

LEVEL	CUT-OFF	DEVIATION
C1–C2	0.6850	± 0.01
C2–C3	0.6550	± 0.05
C3–C4	0.6300	± 0.03
C4–C5	0.6150	± 0.01
C5–C6	0.5750	± 0.05
C6–C7	0.5650	± 0.03

Table 8

Showing Area Under the Curve that is the most significant from C3–C6 levels.

Test Result Variable (s)	Area	Std. Error	p	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
ADC(C1–C2)	0.603	0.084	0.210	0.439	0.768
ADC(C2–C3)	0.692	0.077	0.020	0.541	0.843
ADC(C3–C4)	0.915	0.040	0.000	0.837	0.993
ADC(C4–C5)	0.841	0.055	0.000	0.734	0.949
ADC(C5–C6)	0.811	0.066	0.000	0.682	0.940
ADC(C6–C7)	0.768	0.072	0.001	0.627	0.908

Table 9

Showing the cut off values of ADC at each spinal cord level.

LEVEL	CUT-OFF	DEVIATION
C1–C2	0.9200	± 0.11
C2–C3	1.0350	± 0.12
C3–C4	1.0100	± 0.07
C4–C5	0.9800	± 0.03
C5–C6	1.0450	± 0.11
C6–C7	0.9600	± 0.05

without any visible spinal cord involvement on plain MRI [11] and hence obtain results can be associated with dynamic factors of spinal canal stenosis.

Matamata et al. [12] evaluated 72 patients with spondylosis, out of which 39(54%) without any abnormal signal on T2weighted images showed DTI metrics changes at stenotic segment of the spinal canal, out of the 39 cases 24 cases didn't show any clinical sign signs of myelopathy hence recognizing the early stage of the disease.

Budzik et al. [13] Included 20 symptomatic patients and 15 volunteers in the study. They observed a positive correlation between FA and clinical assessment questionnaire. They observed decrease in FA values was thought to reflect the microstructural disorganization of the cord also assumption was made that if there was not much change in FA it would mean that it was minor lesion and most of the fibrillary microstructures were preserved.

In our study, the mean FA value in the stenotic segments was 0.487, which was lower than the non-stenotic segments 0.729. The ADC values at the stenotic segment were increased with a mean of 1.25 and 0.9 in non-stenotic segments.

Among the 50 patients' of cervical spondylosis, 29 (58%) did not have altered signal intensity on T2WI out of these 13 (44.8%) of cases showed decrease FA values and 11 (42%) of the cases showed increase in ADC values in the narrowed segment of the spinal canal.

European myelopathy score (EMS) is one of the internationally used scores to grade the severity of cervical spondylotic myelopathy and classify into grade 1–3. EMS grading didn't show any significant correlation with age. A total of 23 (46%) patients had grade 1 symptoms of myelopathy indicating early myelopathy changes, out of these 9 (31%) and 7 (26%) showed abnormality on FA and ADC respectively whereas

0% of the patient showed altered signal intensity on T2WI, Hence proving that DTI can detect early stages of myelopathy.

Stenotic segments show a decrease in FA and increase in ADC values in stenotic segments of the spinal cord. Comparison of the values with analysis of variance test (ANOVA) suggested high significance with p-value 0.005 at certain levels.

The comparison between FA, ADC and T2 weighted imaging in the evaluation of spinal cord myelopathy showed the sensitivity was highest in FA values (79%), compared to ADC (71%) and T2 weighted imaging (50%).

5. Conclusion

DTI (ADC with FA) in addition to the routine MRI sequence with detailed clinical history, examination, radiological/clinical diagnosis is a promising tool in:

- Identification of early myelopathy changes before the changes become apparent on routine T2 weighted imaging.
- To accentuate the clinical success of decompression surgery, which would be better when performed early then late.
- Can be used for follow up of a patient with values of FA and ADC, which is numerical, better than T2 weighted imaging. Vedantam and Rajashekar [14] did a review on different classification systems of altered signal intensities in the spinal cord on T2 weighted images, these are all viewer dependent and difficult to follow up.

The potential pitfalls of the study were that, there was no pathological correlation, so the changes become an assumption. The patients could not be followed up for changes in the DTI values to track a worsening in the myelopathy. Post-surgical changes of improvement reflecting the FA and ADC could not be evaluated.

Conflict of interest

None.

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