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RESEARCH

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Diagnostic value of magnetic resonance diffusion tensor imaging in evaluation of cervical spondylotic myelopathy

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Abstract

Background Radiological diagnosis of cervical spondylotic myelopathy should be made as early as possible to obtain favourable clinical outcomes when compared with later stages. Diffusion tensor imaging can reveal early structural changes of the cord in patients with cervical compressive myelopathy.

Aim This study aimed to assess the role of magnetic resonance diffusion tensor imaging in the accurate evaluation of cervical spondylotic myelopathy.

Patients and methods This prospective study included a group of 60 patients with neurological symptoms suggestive for cervical spondylotic myelopathy and a control group of 30 healthy subjects. The clinical severity of compressive myelopathy was assessed based on the European myelopathy score. Magnetic resonance diffusion tensor imaging and tractography were done for all patients and controls.

Results Fractional anisotropy values at the most compressed segments of spinal cord are lower while apparent diffusion coefficient values of the same segments are higher than healthy segments in controls. Fractional anisotropy and apparent diffusion coefficient parameters had higher sensitivity (97.0% and 88.1%, respectively) than conventional T2 WIs (13.4%) and fibre tractography (10%) for the detection of early compressive myelopathy with cutoff values ≤ 0.56 and > 1.23, respectively, in differentiating between patients and control groups.

Conclusion Diffusion tensor imaging indices are valuable tools for quantitative assessment of degenerative cervical spondylotic myelopathy in addition to routine cervical spine magnetic resonance.

Keywords Cervical spondylotic myelopathy, Diffusion tensor imaging, Fractional anisotropy, Apparent diffusion coefficient

Background

Cervical spondylotic myelopathy (CSM) is a cervical spine degenerative condition and is one of the most common causes of spinal dysfunction in adults as well as neurological disorders in the geriatric population [1, 2].

The diagnosis of degenerative cervical myelopathy is based mainly on clinical symptoms and signs of myelopathy in combination with cervical cord pathological changes detected by MRI scan [3].

Magnetic resonance imaging (MRI) is considered the best method for diagnosing cervical spondylotic myelopathy (CSM) through detecting any changes in signal intensity of the spinal cord and thus prediction of outcome and severity of the neurological status in patients with degenerative cervical myelopathy [4].

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However, no correlation exists between findings of MRI and clinical manifestations in most conditions due to inability of MRI to highlight microscopic alterations in the spinal cord associated with CSM, so it cannot give optimum information for accurate disease diagnosis [5].

Diffusion tensor imaging (DTI) is one of the most efficient magnetic resonance imaging (MRI) techniques used to evaluate the diffusion rate of water molecules in live tissues providing a non-invasive tool that can indirectly detect the pathological microstructure of the spinal cord and predicting neurological outcomes [6, 7].

Apparent diffusion coefficient (ADC) measures any diffusion perturbations; increase or restriction. Fractional anisotropy (FA) reveals white matter integrity by expressing the preferred direction of diffusion; its decrease denotes damage and deterioration of the white matter tracts**.** Diffusion tensor tractography (DTT) is other biomarker of DTI providing 3D view of white matter diffusion in the fibre direction [8].

The purpose of this work was to assess the role of MR diffusion tensor imaging (DTI) in the evaluation of cervical spondylotic myelopathy.

Methods

Study population

This prospective study implicated a group of 60 patients with neurological symptoms suggestive for cervical spondylotic myelopathy; 22 of them were males (36.7%) and 38 were females (63.3%) with their ages ranged from 25 to 73 years with a mean of 44.6 ± 12.2 years. They were referred from Neurosurgery department to MRI unit in Radio-diagnosis department over a period from March 2022 to March 2023. A control group of 30 healthy volunteers were also included. Both groups correspond in terms of age and sex to avert bias.

The benefits and risks of the procedure were explained to the patients and volunteers and the study was performed after acquiring institutional review board approval from our hospital and informed consent from them. All patients' data were private and confidential and employed for scientific purpose only.

The inclusion criteria for the patients group were as follows: patients with clinical symptoms consistent with cervical compressive myelopathy with positive or negative previous cervical MRI findings. Regarding the controls, they were completely asymptomatic with no symptoms or signs of cervical spondylotic myelopathy. No age or gender predilection.

Exclusion criteria were as follows: patients with central spinal canal widening, congenital narrowing of spinal canal, and previous spinal surgery, patients other neurological disorders that may affect the results (e.g. inflammation) and any contraindications to MRI examination as any metallic prosthesis.

All included individuals were subjected to *Data collection*

- Full history: personal history, history of current illness, past history of spinal trauma or spinal disease or previous spinal operation.
- Check of all previous radiological examination or investigations.

Clinical examination

At Neurosurgery Department, the patients were classified into grade 1 (mild), grade 2 (moderate) and grade 3 (severe) depending on the European myelopathy score that assesses the myelopathy severity according to 5 functions (gait, hand function, proprioception, paresthesias, and bladder function) [9]. The maximum number of points can be reached in a healthy subject is 18. According to the sum reached in this score, cervical myelopathy is categorized into 3 grades: grade III, 5–8 points; grade II, 9–12 points; and grade I, 13–16 points. Subjects are considered free of signs of cervical myelopathy when having 17 or 18 points [10].

MRI examination

Using 1.5 Tesla GE (General Electric) machine (closed magnet) using a standard cervical coil and in neutral supine position. Patients were asked to avoid moving the head and swallowing during the examination.

The following MRI pulse sequences were included:-

- Sagittal T2 WFSE: TR/TE: 2800–3000/ 110 ms, (FOV): 260 mm, Flip angle 90°, 3,7 mm thickness, NEX: 10 and Matrix: 176 * 200
- Sagittal T1 WFSE: TR/TE: 400/ 8.2 ms, (FOV): 260 mm, Flip angle 90°, 3.7 mm thickness, NEX: 10 and Matrix: 176 * 200
- Axial FFE WI: TR/TE: 500/15 ms, (FOV): 150 mm, Flip angle 25°, 3.7 mm thickness, NEX: 10 and Matrix: 132 * 129

Diffusion tensor imaging MRI (DTI MRI)

A single shot, spin-echo echoplanar sequence in (20–25) encoding directions. A diffusion weighting factor of (*b* value = 0 and 1000 s/mm2). The image was acquired in sagittal plane with image TR/TE: 2800/97

ms, (FOV) of 248 mm, Flip angle 90°, slice thickness of 3.5 mm with no inter-slice gap and Matrix of 80 * 108. To enhance the signal-to-noise ratio and reduce the phase fluctuations, magnitude constructed images were repeated (averages = 4) and temporally averaged.

Image analysis:

- All the images of both groups were resolved by two radiologists; 26 and 15 years of MRI experience, the clinical data and laboratory indicators were unknown for them, in a standard clinical Picture Archiving and Diagnostic System workstation, and final decisions reached by consensus are reported.
- All conventional MRI sequences were resolved for any signs of spinal degenerative diseases or abnormal cord changes.
- In each subject, 5 ROIs were drawn manually within the cervical cord in the sagittal combined anatomical and colour-coded images opposite all cervical disc levels form C2–3 to C6–7.
- Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were calculated from ADC and FA maps of each ROI as a quantitative analysis.
- 3D fibre tractography were created.
- All the obtained data were compared in both groups.

Statistical analysis

The collected data were analysed using Social Sciences (SPSS) version 26 for Windows (IBM Corp., Armonk, N.Y., USA). The Shapiro–Walk test for normality was performed. Qualitative data were symbolized as frequencies and relative percentages. Quantitative data were expressed as mean ± standard deviation (SD). Two groups were compared to each other using the independent samples *T* test and comparisons among three groups were done using one-way ANOVA test (followed by post hoc Tukey or Games–Howell test if significant). Categorical variables (such as sex, disc lesion score) were summarized as counts and percentages. Pearson's Chi-square test was used to calculate difference between qualitative variables and Fisher's exact test or Fisher–Freeman–Halton exact test were used to examine the association between two categorical variables as appropriate. The diagnostic ability of quantitative variable, in prediction of categorical outcome, was calculated using Receiver operating characteristic (ROC) curve. The area under ROC curve (AUC) is graded as follows: 0.90–1 = excellent; 0.80–0.90 = good; 0.70–0.80 = fair; and 0.60–0.70 = poor. Probability (*P* value): significant if *P* value <0.05, insignificant if *P* value > 0.05, and highly significant if *P* value < 0.01.

Results

This prospective study included 2 groups: a group of 60 patients with neurological symptoms suggestive for cervical spondylotic myelopathy and a control group of 30 healthy subjects. The patients were sorted according to the clinical presentation on basis of the European myelopathy score into three categories as follows: 26 patients (43.3%) had grade 1 (mild), 22 patients (36.7%) had grade 2 (moderate) and 12 patients (20%) had grade 3 (severe). The most frequent neurological clinical presentations given by the patients were brachialgia with neck pain seen in 33 patients (55%) and paresthesia in 21 patients (35%).

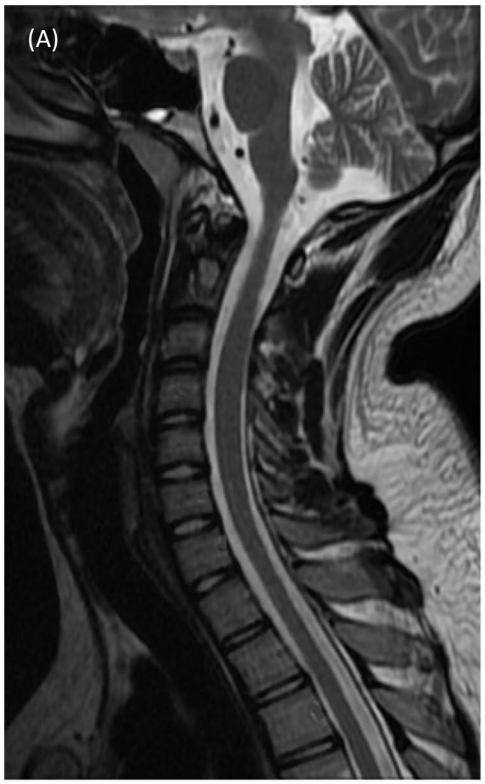
After analysis of all MRI studies for causes of cervical myelopathy, the most common cause was disc lesions detected in all the studied patients (100%). Other causes included cervical malalignment (40%), loss of cervical curvature (28.3%), multiple osteophytosis (18.3%), ossification of ligamentum flavum (13.3%), straightened (Military) cervical spine (10%), partial loss (Hypolordosis) of cervical curvature (6.7%), and ossification of post longitudinal ligament (6.7%). More than one cause could be seen in one patient.

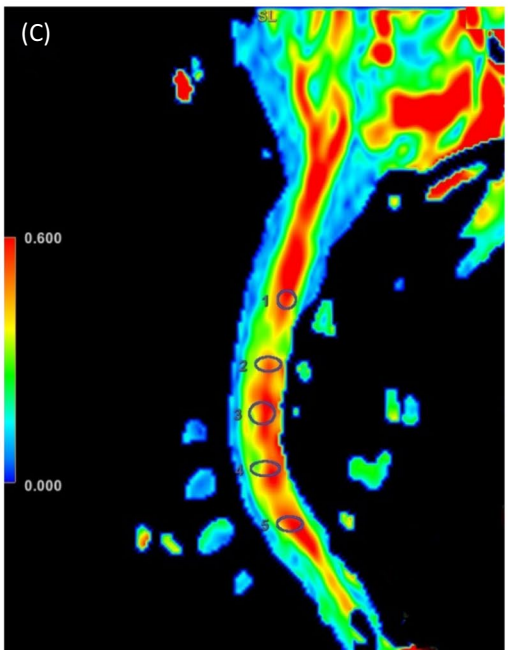
Among the 60 patients with disc disease, 134 cervical intervertebral discs were affected, they were classified according to the type of disc lesion into disc bulge (58 discs; 43.3%), disc protrusion (58 discs; 43.3%), and disc extrusion (18 discs; 13.4%). They were also classified regarding their effect on the spinal cord into **1**; disc not touching the cord (28 discs; 21%), **2**; disc touching the cord (43 discs; 32.08%), **3**; disc indenting the cord (45 discs; 33.5%) and **4**; disc causing cord malacia (18 discs; 13.4%).

The most affected disc was C5–6 (49 patients; 36.5% of the affected discs) followed by C6–7 (30 patients; 22.38% of the affected discs), C4–5 (29 patients; 21.6% of the affected discs), C3–4 (26 patients; 19.4% of the affected discs).

Out of the studied 60 patients in the patients' group, conventional MRI revealed abnormal high signal intensity of the spinal cord on T2 weighted images opposite 18 discs (13.43% of the total affected discs) in 10 patients (15.33% of the studied patients). Four of those patients were grade 2 and 6 of them were grade 3 according to the European myelopathy score as described above.

After qualitative tractographic analysis in both patients and control groups, the white matter tracts of the cord showed a gross normal integrity in all 30 controls (Fig. 1), while in the patients, it showed abnormalities in 6 patients; 5 patients had waist morphology (8.3%) (Fig. 2)

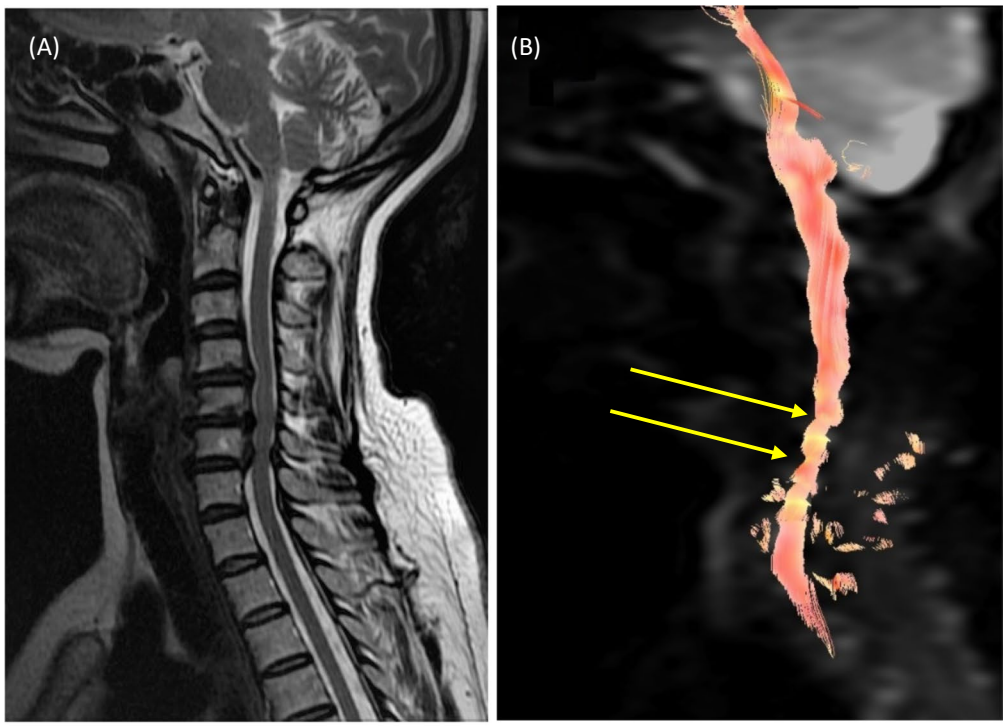


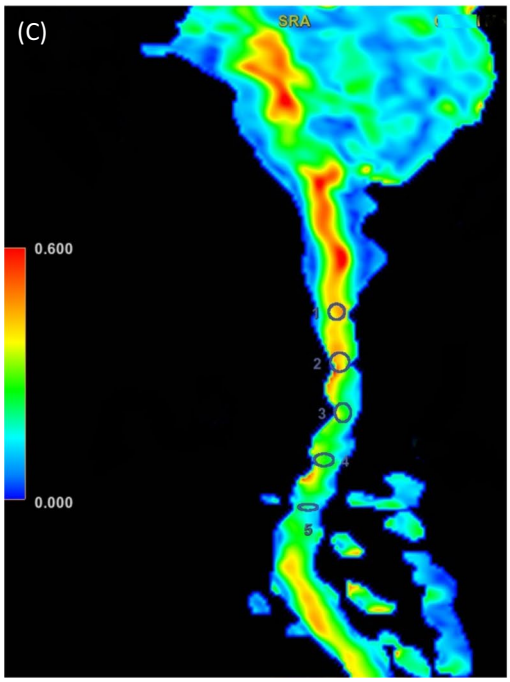


(D)

Name	Disc level	FA value	ADC(e-09mm^2/sec)
ROI 1	C2-3	0.740	0.892 e-09
ROI 2	C3-4	0.613	1.02 e-09
ROI 3	C4-5	0.605	1.01 e-09
ROI 4	C5-6	0.601	.1.03 e-09
ROI 5	C6-7	0.590	1.04 e-09

Fig. 1 A 25-year-old healthy male subject in the control group. **A** Sagittal T2 weighted image showing normal cervical spine curve, no disc disease, no signal intensity alteration of the spinal cord or spinal canal stenosis. **B** Fibre tractography image revealing grossly intact fibre tracts with no significant changes. **C** Sagittal colour-coded DTI image with DTI parameters **D** showing normal FA and ADC values of cervical spinal cord opposite examined cervical discs

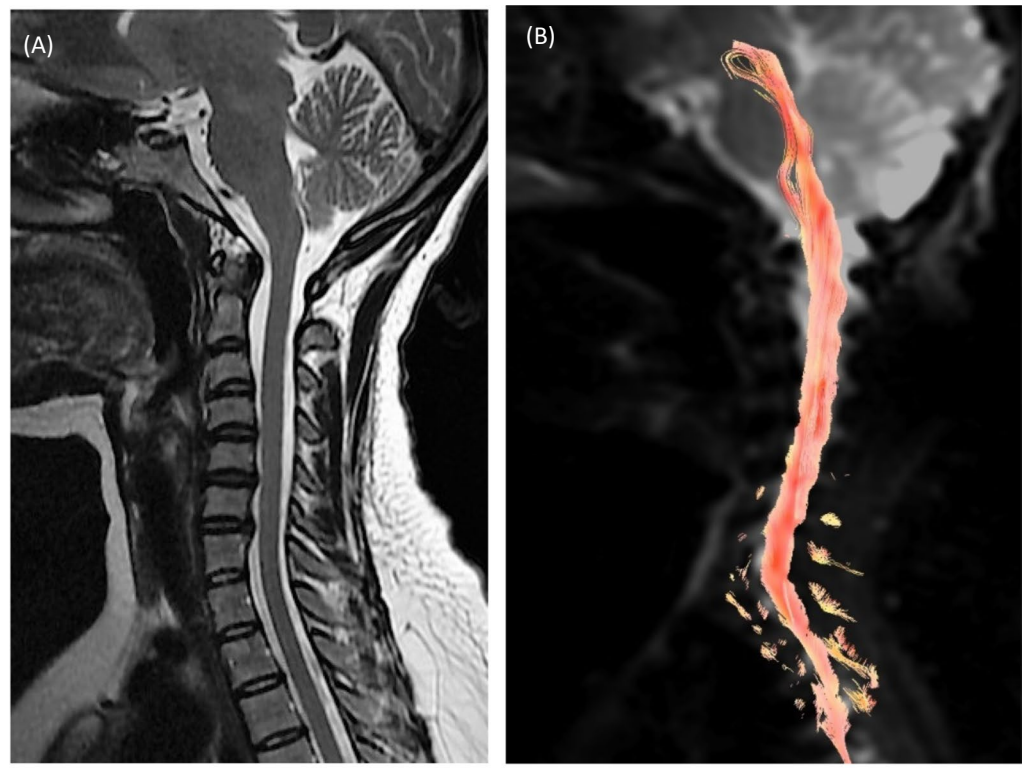




(D)

Name	Disc level	FA value	ADC(e-09mm^2/sec)
ROI 1	C2-3	0.660	1.13 e-09
ROI 2	C3-4	0.560	1.21 e-09
ROI 3	C4-5	0.410	1.59 e-09
ROI 4	C5-6	0.402	1.62 e-09
ROI 5	C6-7	0.299	1.99 e-09

Fig. 2 A 52-year-old male patient presented with moderate symptoms (grade 2 according to the European myelopathy score). **A** Sagittal T2 weighted image showing spastic loss of normal cervical lordosis, diffuse degenerative changes in the form of multiple osteophytes formation and C5/6, C6/7 and to less extent C4/5 central disc protrusion compressing the anterior subarachnoid space and indenting the spinal cord with significant canal stenosis with normal cord signal intensity. **B** Fibre tractography image revealing waist morphology observed at the level of the protruded disc (yellow arrows). **C** Sagittal colour-coded DTI image with DTI parameters **D** showing a significant moderate reduction in FA values opposite C4/5, C5/6 and severe reduction opposite C6/7 disc level as well as increased ADC values opposite the same levels



(D)

Name	Disc level	FA value	ADC(e-09mm^2/sec)
ROI 1	C2-3	0.660	1.12 e-09
ROI 2	C3-4	0.630	1.02 e-09
ROI 3	C4-5	0.615	1.19 e-09
ROI 4	C5-6	0.530	1.43 e-09
ROI 5	C6-7	0.515	1.57 e-09

Fig. 3 A 25-year-old female patient presented with mild symptoms (grade 1 according to the European myelopathy score). **A** Sagittal T2 weighted image showing loss of normal cervical lordosis and C5/6 and C6/7 mild posterior disc bulge compressing ventral subarachnoid space and just touching the spinal cord with normal cord signal intensity. **B** Fibre tractography image revealing grossly intact fibre tracts with no significant changes. **C** Sagittal colour-coded DTI image with DTI parameters **D** showing a mild decrease of FA values opposite C5/6 and C6/7 disc levels and increased ADC value opposite C6/7

and 1 patient had partially interrupted fibre tracts (3.3%). In the remaining 54 patients (90%), the cord appeared normal (Fig. 3).

In the studied targeted patients and control groups, the spinal cord opposite the five cervical intervertebral discs was examined in each subject with a total of 300 levels in patients group and 150 levels in control group.

The mean FA and ADC values of the spinal cord opposite each disc level were measured and compared in control and patient groups. The main FA value was (0.456 ± 0.068) at the level of stenotic segments that was lower than that at the level of unaffected discs in the patients (0.614 ± 0.052) and at the normal discs in controls (0.608 ± 0.042) (Fig. 2, 3) with statistically significant reduction of FA at the level of the stenotic segment (p value 0.001) as illustrated at (Table 1).

Regarding the mean ADC values, it was (1.644 ± 0.285) at the level of stenotic segments that was higher than at the level of unaffected discs in the patients (1.049 ± 0.144) and at the normal discs in controls (1.051 ± 0.123) (Fig. 2, 3) with a statistically significant increase of ADC at the level of the stenotic segment (p value 0.001) as illustrated at (Table 2).

The mean FA value was calculated according to the type of disc lesion

The mean FA was 0.507 ± 0.038 in bulges, 0.431 ± 0.045 in protrusions, and 0.374 ± 0.085 in extrusion. There was a significant difference in FA value between bulge versus protrusion ($P1 < 0.001$) and bulge versus extrusion ($P2 = 0.004$*) but there was no significant difference between protrusion and extrusion ($P3 = 0.191$) (Table 3).

Also, the mean FA value was calculated according to the type of cord affection. There was a significant difference in FA value between bulge not touching the cord versus other types and also between disc touching the cord and disc causing malacia but no significant difference between disc touching the cord and that indenting it or between disc indenting the cord and that causing malacia (Table 3).

After analysis of the FA values in all the studied patients, we made a scoring system for the FA values reduction in abnormal cases where mild FA affection is above 0.5 (54 discs), moderate affection is between

Table 1 FA values in patients and control groups at different cervical spinal cord segments

Disc level	Control	Patients		Statistical tests		
	Normal discs	not Affected disc	Affected disc	Test statistic	*p* value	Post hoc test
C2–3						
N	30	60	0	$T = 1.417$	0.163	–
Mean ± SD	0.652 ± 0.014	0.659 ± 0.022	–			
Min–Max	0.648–0.707	0.620–0.702	–			
C3–4						
N	30	34	26	$F = 50.901$	< 0.001*	$P1 = 0.243$ $P2 < 0.001$* $P3 < 0.001$*
Mean ± SD	0.612 ± 0.005	0.624 ± 0.029	0.458 ± 0.055			
Min–Max	0.601–0.620	0.581–0.660	0.350–0.533			
C4–5						
N	30	30	30	$F = 31.995$	< 0.001*	$P1 = 0.988$ $P2 < 0.001$* $P3 < 0.001$*
Mean ± SD	0.598 ± 0.011	0.596 ± 0.050	0.462 ± 0.064			
Min–Max	0.570–0.612	0.511–0.676	0.355–0.560			
C5–6						
N	30	12	48	$F = 42.360$	< 0.001*	$P1 = 0.392$ $P2 < 0.001$* $P3 = 0.001$*
Mean ± SD	0.590 ± 0.011	0.560 ± 0.050	0.439 ± 0.078			
Min–Max	0.560–0.599	0.513–0.616	0.266–0.580			
C6–7						
N	30	30	30	$F = 13.629$	< 0.001*	$P1 = 0.060$ $P2 < 0.001$* $P3 = 0.001$*
Mean ± SD	0.590 ± 0.077	0.553 ± 0.028	0.476 ± 0.065			
Min–Max	0.500–0.699	0.500–0.599	0.349–0.601			
All levels						
N	150	166	134	$F = 150.897$	< 0.001*	$P1 = 0.673$ $P2 < 0.001$* $P3 < 0.001$*
Mean ± SD	0.608 ± 0.042	0.614 ± 0.052	0.456 ± 0.068			
Min–Max	0.500–0.707	0.500–0.702	0.266–0.601			

F one-way ANOVA test, *SD* standard deviation, *T* independent samples-T test

*Significant at < 0.05. Post hoc test: Games–Howell test; p1: *p* value from post hoc test comparing control and not affected discs; p2: *p* value from post hoc test comparing control and affected discs; p3: *p* value from post hoc test comparing not affected and affected discs

Table 2 ADC values in patients and control groups at different cervical spinal cord segments

Disc level	Control	Patients		Statistical tests		
	Normal discs	not affected disc	Affected disc	Test statistic	*p* value	Post hoc test
C2–3						
N	30	60	0	T = 0.213	0.832	–
Mean ± SD	0.945 ± 0.082	0.949 ± 0.071				
Min–Max	0.844–1.050	0.810–1.240				
C3–4						
N	30	34	26	F = 28.731	< 0.001*	P1 = 0.670 P2 < 0.001* P3 < 0.001*
Mean ± SD	1.038 ± 0.023	1.023 ± 0.070	1.630 ± 0.279			
Min–Max	0.999–1.090	0.878–1.130	1.120–2.060			
C4–5						
N	30	30	30	F = 48.167	< 0.001*	P1 = 0.087 P2 < 0.001* P3 < 0.001*
Mean ± SD	1.097 ± 0.063	1.189 ± 0.115	1.687 ± 0.231			
Min–Max	1.010–1.190	1.050–1.400	1.120–2.050			
C5–6						
N	30	12	48	F = 21.953	< 0.001*	P1 = 0.521 P2 < 0.001* P3 < 0.001*
Mean ± SD	1.171 ± 0.037	1.117 ± 0.114	1.607 ± 0.317			
Min–Max	1.110–1.230	1.030–1.290	1.080–2.050			
C6–7						
N	30	30	30	F = 29.885	< 0.001*	P1 = 0.209 P2 < 0.001* P3 < 0.001*
Mean ± SD	1.003 ± 0.186	1.109 ± 0.194	1.675 ± 0.305			
Min–Max	0.874–1.580	0.920–1.720	1.070–2.140			
All levels						
N	150	166	134	F = 136.534	< 0.001*	P1 = 0.992 P2 < 0.001* P3 < 0.001*
Mean ± SD	1.051 ± 0.123	1.049 ± 0.144	1.644 ± 0.285			
Min–Max	0.844–1.580	0.810–1.720	1.070–2.140			

F One-way ANOVA test, *SD* standard deviation, *T* Independent Samples-T test

*Significant at < 0.05. Post hoc test: Games–Howell test; p1: *p* value from post hoc test comparing control and not affected discs; p2: *p* value from post hoc test comparing control and affected discs; p3: *p* value from post hoc test comparing not affected and affected discs

Table 3 The mean FA value at the level of stenotic segments according to the type of disc lesion and cord affection (*n* = 134)

	N	Mean ± SD	Min–Max	*F*	*p* value	Post hoc test
Disc lesion						
Bulge	58	0.507 ± 0.038	0.389–0.601	31.594	< 0.001*	P1 < 0.001 P2 = 0.004* P3 = 0.191
Protrusion	58	0.431 ± 0.045	0.299–0.580			
Extrusion	18	0.374 ± 0.085	0.266–0.555			
Disc affection						
Bulge not touching cord	28	0.570 ± 0.028	0.560–0.620	25.002	< 0.001*	P4 = 0.001* P5 < 0.001* P6 = 0.008* P7 = 0.087 P8 = 0.025* P9 = 0.074
Disc touching the cord	43	0.469 ± 0.049	0.350–0.521			
Disc indenting the cord	45	0.433 ± 0.051	0.349–0.580			
Disc causing malacia in MRI	18	0.328 ± 0.067	0.266–0.433			

F one-way ANOVA test, *SD* standard deviation

*Significant at < 0.05. Post hoc test: Games–Howell test; p1: *p* value: bulge vs. protrusion, p2: *p* value: bulge vs. extrusion, p3: *p* value: protrusion vs. extrusion, p4: *p* value: bulge not touching the cord vs. touching the cord, p5: *p* value: bulge not touching the cord vs. indenting the cord, p6: *p* value: bulge not touching the cord vs. malacia, p7: *p* value: bulge touching the cord vs. indenting the cord, p8: *p* value: bulge touching the cord vs. malacia, p9: *p* value: disc indenting the cord vs. malacia

0.3 and 0.5 (74 discs) while severe affection is below 0.3 (6 discs). The distribution of FA values scoring system in abnormal discs according to the type of disc lesion revealed that 84.48% of disc bulge lesions were mild, 89.66% of disc protrusion lesions were moderate and 72.22% of disc extrusion lesions were moderate with highly significant p value (< 0.001). The distribution of FA values scoring system in abnormal discs according to the cord affection revealed that most of the disc bulge lesions not touching the cord were mild, most of the disc lesions touching, indenting the cord, and discs causing cord malacia were moderate (Table 4).

The sensitivity and specificity of fractional anisotropy and apparent diffusion coefficient in the seat of detecting myelopathy were detected in both groups after ROC analysis which showed an area under the curve indicated by the cutoff values proposed for each level. The ROC for FA gives AUC 0.969 with sensitivity and specificity of 97% and 92.7%, respectively, while ADC gives AUC 0.958 with sensitivity and specificity 88.1%

Table 4 Distribution of FA values scoring system in abnormal discs according to the type of disc lesion and cord affection

	Mild (> 0.5) (*n* = 54)	Moderate (> 0.3–0.5) (*n* = 74)	Severe (0–0.3) (*n* = 6)	*P* value
Disc lesions				
Bulge (*n* = 58)	49 (84.48%)	9 (15.51%)	0 (0.0%)	< 0.001*
Protrusion (*n* = 58)	4 (6.9%)	52 (89.66%)	2 (3.44%)	
Extrusion (*n* = 18)	1 (5.55%)	13 (72.22%)	4 (22.22%)	
Cord affection				
Bulge not touching cord (*n* = 28)	26 (92.86%)	2 (7.14%)	0 (0.0%)	< 0.001*
Disc touching the cord (*n* = 43)	20 (45.45%)	23 (53.48%)	0 (0.0%)	
Disc indenting the cord (*n* = 45)	8 (18.2%)	37 (82.22%)	0 (0.0%)	
Disc causing malacia in MRI (*n* = 18)	0 (0.0%)	12 (66.7%)	6 (33.3%)	

*Significant at $p < 0.05$

Table 5 The diagnostic performance of FA value in differentiating between patients and controls in all levels (based on ROC curve analysis)

Disc FA	Cutoff	AUC	SE	*P* value	95% CI	Sens	Spec	PPV	NPV	Accuracy
All levels	≤ 0.56	0.969	0.011	< 0.001*	0.948 to 0.990	97.0	92.7	85.5	98.6	94.0
C3–4	≤ 0.533	1.000	0.000	< 0.001*	1.000 to 1.000	100.0	100.0	100.0	100.0	100.0
C4–5	≤ 0.56	0.985	0.011	< 0.001*	0.963 to 1.000	100.0	91.1	78.9	100.0	93.3
C5–6	≤ 0.521	0.992	0.009	< 0.001*	0.974 to 1.000	95.8	100.0	100.0	96.8	98.1
C6–7	≤ 0.555	0.813	0.068	< 0.001*	0.680 to 0.947	93.3	70.0	60.9	95.5	77.8

AUC area under the ROC curve, *CI* confidence interval of AUC, *NPV* negative predictive value, *PPV* positive predictive value, *SE* standard error of AUC, *Sens* sensitivity, *Spec.* specificity; *p* value: from a test comparing the observed AUC to the null hypothesis AUC of 0.5

*Significant at $p < 0.05$; Sensitivity, specificity, and predictive values are expressed as percentages

Table 6 The diagnostic performance of ADC value in differentiating between patients and controls in all levels (based on ROC curve analysis)

Disc ADC	Cutoff	AUC	SE	*P* value	95% CI	Sens	Spec	PPV	NPV	Accuracy
All levels	> 1.23	0.958	0.014	< 0.001*	0.931 to 0.986	88.1	98.0	95.2	94.8	94.9
C3–4	> 1.09	1.000	0.000	< 0.001*	1.000 to 1.000	100.0	100.0	100.0	100.0	100.0
C4–5	> 1.19	0.967	0.024	< 0.001*	0.921 to 1.000	93.3	97.8	93.3	97.8	96.7
C5–6	> 1.23	0.853	0.070	< 0.001*	0.716 to 0.989	83.3	100.0	100.0	88.2	92.6
C6–7	> 1.46	0.959	0.028	< 0.001*	0.905 to 1.000	86.7	96.7	92.9	93.5	93.4

AUC area under the ROC curve, *CI* confidence interval of AUC, *NPV* negative predictive value, *PPV* positive predictive value, *SE* standard error of AUC, *Sens* sensitivity, *Spec* specificity, *p* value: from a test comparing the observed AUC to the null hypothesis AUC of 0.5

*Significant at $p < 0.05$; Sensitivity, specificity, and predictive values are expressed as percentages

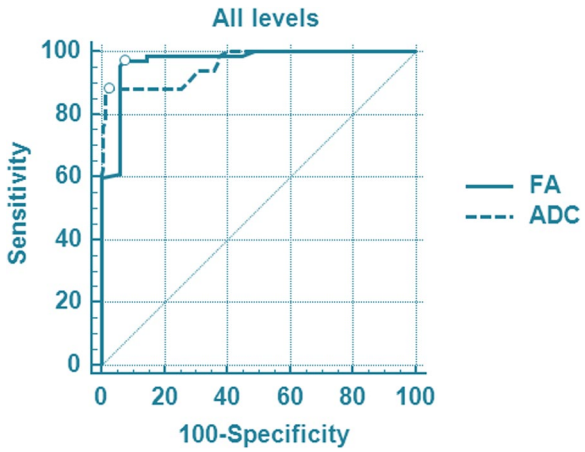


Fig. 4 ROC curve for the diagnostic performance of FA (continuous line) and ADC (dotted line) at all disc levels

and 98.0%, respectively, as shown in (Tables 5, 6) and (Fig. 4).

Regarding to the final outcome of the studied patients depending on clinical presentation, imaging findings, and clinical follow-up, the diagnostic accuracy of the T2WI, tractography, FA, and ADC for the study-based statistical analysis is shown in (Table 7).

Discussion

The goal of our study was to discuss the advantage of MR diffusion tensor imaging, depending on its quantitative and qualitative parameters, in detecting the microstructural changes of spinal cord in cervical spondylotic myelopathy (CSM) patients even with no intramedullary changes on cMRI. It was carried out on 60 patients presenting with neurological symptoms of CSM. To avoid bias, a control group was included that was age/sex-matched to the patients.

Among the 60 studied patients, the mean age of these patients was 44.6 ± 12.2 years (range 25 to 73 years) with female predominance (63.3%). The majority of them were in the age group of 51 to < 60 Years. In Schöller et al. [11] study, the prevalence of degenerative spine pathology increased after the age of 50 years. Also, Nouri et al. [12] reported that about 60% of people above 40 years old suffered from CSM. The included patients were sorted clinically according to the European myelopathy score (EMS) in-agreement with the studies of Nukala et al. [13] and Schöller et al. [11].

In agreement with Wang et al. [14] and Rajasekaran et al. [15], we used a control group in our study for comparing FA and ADC values with patients' group. We obtained FA and ADC values at cervical spinal cord segments opposite all cervical disc levels taking in mind avoiding partial volume effect of CSF.

By conventional MRI, the examined 300 cervical discs were categorized according to the type of disc lesion as well as its effect on spinal cord. Qualitative analysis was based on the presence and absence of high signal intensity of the affected cord on T2 weighted images. Out of the 60 patients, 10 patients (15.33%) having 18 discs (13.4%) showed signal changes on T2 weighted images as high signal intensity.

Fibre Tractography (FT) is an important DTI parameter that uses specialized tracing algorithms to get a 3D reconstruction of white matter tracts in the central nervous system [16]. In the 60 patients with CSM, 6 patients (10%) had abnormalities in cord integrity; waist morphology in 5 patients and partial interruption in 1 patient. The remaining 54 patients had grossly normal spinal cord on qualitative tractographic analysis. This agrees with Lee et al. [17] who suggested that DTI tractography techniques cannot explore the full damage of the spinal cord fibres with unexpected no significant difference in between neurologically worse and neurologically better examined groups.

Fractional anisotropy (FA) is the most commonly used DTI parameter to indicate microstructural integrity by measuring the spread of water in a preferred direction within a group of axons. It ranges from 0 to 1. In unidirectional diffusion, the FA value approaches 1, whereas in isotropic diffusion (i.e. free in all directions), its value equals 0. The reduction in the FA value is due to white matter tracts damage and degradation [18, 19]. Apparent diffusion coefficient is another helpful parameter that quantitatively expresses the free diffusion of water in the extracellular space and is expressed in mm^2 /s. Changes in its value are proportional to the intensity of diffusion in a given area [18].

Table 7 Diagnostic accuracy of T2 weighted image, tractography, FA, and ADC depending on statistical analysis

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
T2W1	13.4	100.0	100.0	72.1	73.3
Tractography	10.0	100.0	100.0	52.6	55.0
ADC	88.1	98.0	95.2	94.8	94.9
FA	97.0	92.7	85.5	98.6	94.0

In concordance with Guan et al. [20] and Gopinath et al. [21], quantitative analysis was done and we reported that CSM patients had significant FA decrease and ADC increase at the most compressed parts of the spinal cord. By One-way ANOVA test Our study revealed that the mean FA value and ADC value were (0.456 and 1.644), respectively, in affected segments compared to (0.614 and 1.049) in unaffected segments and (0.608 and1.051) in healthy segments in the control group, respectively.

Mostafa et al. [22] found a statistically significant reduction of FA values (0.57 ± 0.10 vs. 0.67 ± 0.06) and an increase in ADC values (1.02 ± 0.34 vs. 0.88 ± 0.31). Guan et al. [20] showed that the mean FA value was 0.45 in stenotic segments compared to 0.57 in non-stenotic segments and the mean ADC value was 2.1 in stenotic segments compared to 1.3 in non-stenotic segments. Iwasaki et al. [23] reported that the mean FA value was 0.56 in stenotic segments compared to 0.8 in non-stenotic segments and He et al. [24] concluded that the mean FA value was 0.49 in stenotic segments compared to 0.61 in non-stenotic segments.

The mean FA value was measured in each disc lesion. There was a significant difference in FA value between bulge versus protrusion and bulge versus extrusion but no significant difference between protrusion and extrusion by Post hoc test.

The mean FA value was measured in each cord affection type and was compared by Post hoc test. There was a significant difference in FA value between bulge not touch cord versus other cord affection score and also between disc touching cord and disc causing malacia but no significant difference was found between disc touching cord versus indenting or between indenting versus disc causing malacia.

In the present study, a virtual scoring system was made to estimate the severity of myelopathy according to FA values reduction in patient group. It was used in similar studies like those of Ellingson et al. [25] and Hassan et al. [26] so that mild FA affection is between 0.5 to 0.6, moderate affection is between 0.3 and 0.5 while severe affection is below 0.3. This scoring system was done in order to give approximate picture of the gradations of the reduction in FA values.

This was in agreement with Facon et al. [27], Song et al. [28], Hori et al. [29], Hassan et al. [26] and Liu et al. [30] who reported a significant FA differences between compressed and non-compressed cord. This reduction is attributed to axonal damage, local extracellular oedema or reduction in nerve fibres with increased extracellular space. Our study showed that FA values had significant reduction by different statistical tests in abnormal discs which became more reduced with the advancement of disc lesion severity, so, the more compressed the cord is, the more reduction in FA values are obtained ($p = 0.001$).

We noticed elevated FA values in some mild discs bulges not touching the cord in comparison with normal discs, this could be attributed to either early modification of the extracellular compartment or intracellular oedema with an inflow of extracellular water reducing the extracellular space or secondary to inflammation or mechanical compression as reported by Facon et al. [27]. In the rest of the discs with mild bulges in our study, FA values showed a significant reduction. Banaszek et al. [31] reported significant differences in FA values between the controls and subjects with cervical spondylosis, including patients with early stage who had no spinal cord compression on plain MRI scans.

We also noticed that FA value at a level below the most affected disc was decreased with or without elevation at the ADC value. Most decreases in FA value were noted at C6/C7 level as C5/6 level is the most affected disc matching with Suetomi et al. [32] who noticed that C6/C7 showed the minimum FA even if not compressed or distant from the lesion. Therefore, the results of their study indicate that the FA value is not useful as an objective diagnostic indicator of the segmental level of myelopathy alone. d'Avanzo et al. [33] also reported that FA represents a promised diagnostic tool in patients affected with CSM through detecting early cervical myelopathy.

Also, Guan et al. [20] observed a significant reduction of FA at the most compressed level as well as at sites away from affected disc. This is explained by the CSM-associated demyelination and axonal damage that affect both the myelopathic lesion and the distal sites especially with chronicity. Thus, the diffusion indices from the whole cervical spinal cord could be selected to reflect overall damage in CSM patients comprehensively.

Our study showed higher sensitivity of FA and ADC parameters than conventional T2WIs and DT tractography for detection of early compressive myelopathy. FA sensitivity and specificity were 97.0% and 92.2%, respectively, and ADC sensitivity and specificity were 88.1% and 98%, respectively, conventional T2 WIs sensitivity and specificity were 13.4% and 100%, respectively, and DT tractography sensitivity and specificity were 10% and 100%, respectively.

Nukala et al. [12] reported that FA sensitivity and specificity in recognition of myelopathy changes were 78.8% and 79.7%, respectively, and ADC sensitivity and specificity were 71.4% and 62.1%, respectively. Our results agree with Dong et al. [34], Shen et al. [35] and Zhang et al. [36], who reported a higher sensitivity of DTI quantitative parameters than conventional MRI in the detection of early compressive myelopathy.

This study was limited by the difficulty of following up the changes in the DTI values to track deterioration of myelopathy.

Conclusions

This study recognized that DTI, with its quantitative biomarkers, has a pivotal role in assessment of CSM when used as a complement to routine cervical spine MRI. These parameters (FA value is more sensitive than ADC) are useful in detecting myelopathy even in patients with a mild grade EMS score and thus can be used as a stepping stone for the treatment plane.

Diffusion tensor imaging is recommended to be used as a routine examination for estimating the assessment of the spinal cord following cervical spondylosis complementary to cMRI for better evaluation of white matter integrity and microstructural changes and thus future decision-making regarding conservative management versus surgical intervention in CSM patients.

Abbreviations

ADC	Apparent diffusion coefficient
CSM	Cervical spondylotic myelopathy
cMRI	Conventional magnetic resonance imaging
DTI	Diffusion tensor imaging
DTT	Diffusion tensor tractography
EMS	European myelopathy score
FT	Fibre tractography
FA	Fractional anisotropy
ROI	Region of interest

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Author contributions

OA suggested the research idea, ensured the original figures and data in the work, minimized the obstacles to the team of work, correlated the study concept and design and had the major role in analysis; NS collected data in all stages of manuscript and performed data analysis. HA supervised the study with significant contribution to design the methodology, manuscript revision and preparation. EA correlated the clinical data of patient and matched it with the findings, drafted and revised the work. All authors read and approved the final manuscript for submission.

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Availability of data and materials

The author's confirm that all data supporting the finding of the study are available within the article and the raw data and data supporting the findings were generated and available at the corresponding author on request.

Declarations

Ethics approval and consent to participate

Informed written consents taken from the patients and healthy volunteers, and the study was approved by ethical committee of Tanta university hospital, faculty of medicine. Committee's reference number: 35214/1/22.

Consent for publication

All participants included in the research gave written consent to publish the data included in the study.

Competing interests

The authors declare that they have no competing of interests.

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