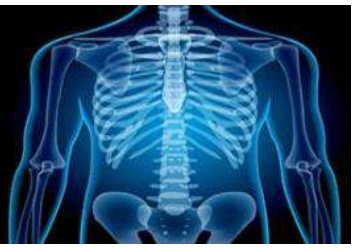
International Journal of Radiology and Diagnostic Imaging



E-ISSN: 2664-4444
P-ISSN: 2664-4436
www.radiologypaper.com
IJRDI 2021; 4(2): 116-123
Received: 19-02-2021
Accepted: 21-03-2021

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Role of diffusion tensor imaging (DTI) as a quantitative diagnostic tool in assessing cervical spondylotic myelopathy

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DOI: http://dx.doi.org/10.33545/26644436.2021.v4.i2b.207

Abstract
Aims and Objectives: To compare fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values obtained by DTI in stenotic and non-stenotic cervical spinal segments of patients with clinical evidence of cervical spondylotic myelopathy.
Materials and Methods: A prospective study was conducted among 50 individuals over a period of 18 months. MRI of cervical spine was performed in patients referred/admitted to the institution with clinical suspicion of cervical spondylotic myelopathy. The protocol included: 2D sagittal T1WI, T2WI, STIR sequence, axial T2WI, T1WI, coronal STIR sequence and axial DTI sequences. Post-processing was done using Philips FIBRETRAK software.
Results: In the study there was significant decrease in the values of FA at the levels with canal stenosis and a FA cut-off value ≤0.459 had sensitivity of 100% and specificity of 85.6% for diagnosing cervical spondylotic myelopathy. Similarly, there was a significant increase in the ADC value at the stenotic levels and the cut-off value >1.3265 x 10^{-3} mm^2/s had a sensitivity of 100% and a specificity of 76%.
Conclusions and Recommendations: DTI can thus be used as an efficient tool in early diagnosis of cervical spondylotic myelopathy in patients where there are no obvious changes in the signal intensity of the cord.

Keywords: diffusion tensor imaging (DTI), fractional anisotropy (FA), apparent diffusion coefficient (ADC), cervical spondylotic myelopathy

1. Introduction
Degenerative cervical spine disorder is a common non-traumatic disorder of the spine in the middle aged and elderly population. Conventional magnetic resonance imaging (MRI) with T2 weighted sequence is often used as the imaging modality of choice in identifying spondylosis and its complications. However, high signal changes of the spinal cord on T2 weighted image occurs only late in the course of the disease. Diffusion tensor imaging (DTI) is a relatively new MRI technique which is sensitive to the diffusion of water molecules and reflects the microscopic structural organization of white matter fibres. A change in the diffusion from anisotropic diffusion to isotropic diffusion can be evaluated using ADC (apparent diffusion coefficient) and FA (fractional anisotropy). An increase in the ADC value signifies that the medium has isotropic diffusion. FA varies between 0 (isotropic) and 1 (infinite anisotropic diffusion).
The objectives of this study was to obtain fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values in stenotic and non-stenotic cervical spinal segments of patients with clinical evidence of cervical spondylotic myelopathy and to compare the same in order to assess the value of DTI parameters in early detection of cervical spondylotic myelopathy.

2. Materials and Methods
- Study Design: Prospective Study
- Study Duration: 18 months (October 2018 – June 2020)
- Sample size: 50
- Inclusion Criteria: Patients referred/admitted to the institution with clinical suspicion of cervical spondylotic myelopathy.

- Exclusion Criteria:
  - Spine surgery or hardware for treatment of spinal injury within the scanning field.
  - Pregnancy
  - Patients with spinal cord tumours or traumatic injury to the spinal cord that would affect DTI parameters.
- Protocol: 2D sagittal T1WI, T2WI, STIR, axial T2WI, T1WI, coronal STIR and axial DTI sequences. Post-processing was done using Philips FIBRETRAK software.

Conventional MR sequences

Sequence	Spin echo sequences
Position	Supine, head first
FOV	224 x 224mm
Slice thickness	4mm section
Slice interval	0.3mm

Diffusion Tensor Sequence

Slice plane	Axial
Slice thickness	2mm section
Slice interval	0mm
Reconstruction matrix	176 x176
EPI factor	33
NSA	5
b factor	0-800mm^2/s
Sequence duration	4 minutes 25seconds

3. Results and Discussion

3.1 Age and Sex distribution

In our study, the maximum prevalence of cervical spondylosis was seen between 5th and 6th decade (Table 1, Figure 1) with a higher prevalence in males (62%) (Table 2, Figure 2).

3.2 Grades and levels of stenosis

Among the study population, 24.5% had single level canal stenosis and 75.5% had multi-level canal stenosis (Table 3, Figure 3).

Out of a total of 104 stenotic segments, grade I stenosis (partial obliteration of the subarachnoid space) was most common (87.5%), followed by grade II stenosis (complete obliteration of the subarachnoid space) (10.5%). Grade III stenosis (cervical cord compression or displacement with increased cord signal intensity) was observed in only 2% of the study population (Table 4, Figure 4). This was in comparison to the study conducted by Nukala *et al* which included 50 symptomatic patients of which 7 individuals had grade 2 CSM (cervical spondylotic myelopathy) and 14 individuals had grade 3 CSM [1].

3.3 Distribution of most stenotic level

The maximum level of compression was taken into account in each subject and evaluated. 40.8% had the most stenotic level at C4-C5 level, followed by the C5-C6 level (28.5%) (Table 4, Figure 4). Also the mean canal diameter was found to be the lowest at C4-C5 level (9.47mm) and highest at C2-C3 level (11.49mm). Hence, in our study, we concluded that the C4-C5 level is the most commonly involved level for cervical myelopathy and the narrowest level. The study conduct by K RoseBist *et al* however showed maximum decrease in canal space at C3-C4 levels [2].

3.4 Comparison of mean FA

The mean FA at stenotic segments was 0.3554 ± 0.198 and the mean FA in non-stenotic segments was 0.6468 ± 0.188 (Table 6). This was similar to the study conducted by Nukala *et al* which revealed a mean FA value of 0.48 in stenotic segment compared to 0.729 in non-stenotic segments [1].

3.5 Comparison of Mean ADC

The mean ADC at stenotic segments was 1.9705 ± 0.819 x 10^{-3} mm^2/s and the mean ADC in non-stenotic segments was 1.1088 ± 0.612 x 10^{-3} mm^2/s (Table 7). This was similar to the study conducted by Toktas *et al* which revealed that the mean ADC in the stenotic cervical segments was 1.312 ± 0.2405 x 10^{-3} mm^2/s and in the non-stenotic cervical segments was 0.9183 ± 0.1477 x 10^{-3} mm^2/s [3].

3.6 Correlation of Fractional Anisotropy amongst stenotic and non stenotic segments:

In our study, there was a significant difference between mean FA at stenotic and non-stenotic segments in C3-C4, C4-C5, C5-C6, and C6-C7 levels but there was no significant difference in values at C2-C3 level (Table 8, Figure 6). This is a measure of anisotropic diffusion, which happens in one direction and in an orderly fashion in white matter tracts in normal physiological conditions. The results were similar to the study by Banszek *et al* which showed a decrease in FA values in stenotic segments of the spinal cord with significant difference between stenotic and non-stenotic groups [4].

3.7 Correlation of Apparent Diffusion Coefficient values amongst stenotic and non stenotic segments

In our study, a comparison between the mean ADC values at stenotic and non-stenotic demonstrated that there was a significant difference in the ADC values among stenotic and non-stenotic segments in C3-C4, C4-C5, C5-C6, and C6-C7 levels but at C2-C3 level there was no significant difference (Table 9, Figure 7). The increase in ADC values could be attributed to the isotropic diffusion of water molecules, which increases in patients with myelopathy. This result was similar to the study by Nukala *et al* which showed an increase in ADC values in stenotic segments of the spinal cord [1].

3.8 Correlation between grade of compression and FA & ADC at the most stenotic level

We found that there is a weak negative correlation [correlation coefficient -0.181] between the grade of compression and the fractional anisotropy which however was not statistically significant (p>0.05). This was in contrast to the study conducted by Lee *et al* where they found a significant negative correlation between the grades of compression (p<0.001) [5].

Similarly, although there was a weak positive correlation [correlation coefficient 0.112] between the grade of compression and apparent diffusion coefficient, it was also not statistically significant (p>0.05). This was similar to the results of the study by Lee *et al* where they did not establish a correlation between the grades of compression and ADC values [5].

3.9 Correlation between the cervical canal diameter and FA values in stenotic and non stenotic groups

In both stenotic and non-stenotic population in our study, there was no significant correlation between the canal diameter and the FA values (p>0.05). This was in contrast to the study conducted by Banszek *et al* which revealed a significant positive correlation between the mean FA value and spinal canal AP diameter [4].

3.10 Correlation between the cervical canal diameter and ADC values in stenotic and non stenotic groups

In the non stenotic group there was weak positive correlation between the canal diameter and the ADC values at C3-C4 level with a correlation coefficient of 0.38 (p<0.05). At other levels in the non stenotic group there was no statistically significant correlation between canal diameter and the ADC values (p>0.05). In stenotic population, our study did not reveal a statistically significant correlation between ADC and canal diameter at any level (p>0.05). This was again in contrast to the study conducted by Banszek *et al* which revealed a significant negative correlation between the mean ADC value and spinal canal AP diameter [4].

3.11 Validity of FA and ADC in diagnosing cervical spondylotic myelopathy

By taking the confidence interval of 95% and assessing the FA values, we derived that FA ≤ 0.4590 had the highest sensitivity of 100% and specificity of 85.6% in diagnosing compressive myelopathy. This result was similar to the study conducted by Rajasekaran *et al* which showed a significantly decreased FA (0.49 ± 0.081) at stenotic segments [6].

By taking the confidence interval of 95% and assessing the ADC values, we derived that ADC >1.3265 x 10^{-3} mm^2/s had a high sensitivity of 96.2% and a specificity of 76% in diagnosis of compressive myelopathy. This was similar to the study conducted by Rajasekaran *et al* which showed a significantly increased ADC (1.8 ± 0.315 x 10^{-3} mm^2/s) at stenotic segments [6].

Our study also revealed that the T2WI performed poorly in recognizing myelopathy changes in grade 1 stenosis (0%) while FA and ADC fared better at recognizing myelopathic changes which was comparable to the results obtained by Nukala *et al* which also showed that T2WI did not reveal myelopathic changes in grade 1 disease.

Table 1: Age distribution of subjects

Age	Count	Percentage
<30 years	6	12.0%
31 to 40 years	9	18.0%
41 to 50 years	12	24.0%
51 to 60 years	19	38.0%
>60 years	4	8.0%
Total	50	100%

Table 2: Sex distribution of subjects

Sex	Count	Percentage
Female	19	38.0%
Male	31	62.0%
Total	50	100%

Table 3: Distribution of stenosis among subjects

Stenosis	Count	Percentage
Single level	12	24.5%
Multilevel	37	75.5%
Total	49	100.0%

Table 4: Distribution of grade of stenosis.

Grade of Compression	Count	Percentage
I	91	87.5%
II	11	10.5%
III	2	2%

Table 5: Distribution of most stenotic level

Most Stenotic Level	Count	Percentage
C2-C3	1	2.0%
C3-C4	6	12.2%
C4-C5	20	40.8%
C5-C6	14	28.5%
C6-C7	8	16.3%

Table 6: Comparison of mean FA values between stenotic and non stenotic segments.

Stenosis		N	Mean	Std. Deviation	Std. Error Mean	p value
FA	Present	104	.3554	.09975	.00978	<0.0001
	Absent	146	.6468	.09447	.00782	

Table 7: Comparison of mean ADC values between stenotic and non stenotic segments.

Stenosis		N	Mean	Std. Deviation	Std. Error Mean	p value
ADC	Present	104	1.9705	.40918	.04012	<0.0001
	Absent	146	1.1088	.30640	.02536	

Table 8: Comparison of FA values at stenotic and non stenotic segments of each intervertebral level.

	Stenosis	Count	Mean	SD	Median	Minimum	Maximum	p
FA at C2-C3	Absent	49	.67	.10	.66	.51	.89	
	Present	1	.34	.	.34	.34	.34	
FA at C3-C4	Absent	34	.66	.09	.66	.50	.85	<0.0001
	Present	16	.39	.07	.41	.30	.49	
FA at C4-C5	Absent	10	.66	.08	.67	.56	.79	<0.0001
	Present	40	.37	.10	.39	.16	.56	
FA at C5-C6	Absent	18	.62	.10	.59	.49	.80	<0.0001
	Present	32	.33	.10	.33	.13	.48	
FA at C6-C7	Absent	35	.61	.08	.60	.46	.79	<0.0001
	Present	15	.33	.12	.35	.16	.48	

Table 9: Comparison of ADC values at stenotic and non stenotic segment of the different levels of cervical vertebrae.

	Stenosis	Count	Mean	SD	Median	Minimum	Maximum	p value
ADC at C2-C3	Absent	49	1.05	.28	1.01	.50	1.77	
	Present	1	1.94	.	1.94	1.94	1.94	
ADC at C3-C4	Absent	34	1.08	.25	1.02	.69	1.78	<0.0001
	Present	16	1.91	.18	1.96	1.44	2.33	
ADC at C4-C5	Absent	10	1.18	.39	1.08	.78	1.77	<0.0001
	Present	40	1.99	.37	1.87	1.54	3.16	
ADC at C5-C6	Absent	18	1.29	.36	1.33	.66	1.76	<0.0001
	Present	32	2.02	.50	1.97	.67	3.52	
ADC at C6-C7	Absent	35	1.11	.31	1.06	.59	1.74	<0.0001
	Present	15	1.87	.50	1.94	.90	2.90	

Table 10: Validity of FA in diagnosis of compressive myelopathy

Area under the ROC curve	0.995
Standard error	0.003
95% Confidence interval	0.990 to 1.000
Associated criterion	≤0.4590
Significance level	< 0.0001

Table 11: Validity of ADC in diagnosis of compressive myelopathy.

Area under the ROC curve	**0.962**
Standard error	0.015
95% Confidence interval	0.933 to 0.990
Associated criterion	≥1.3265
Significance level	< 0.0001

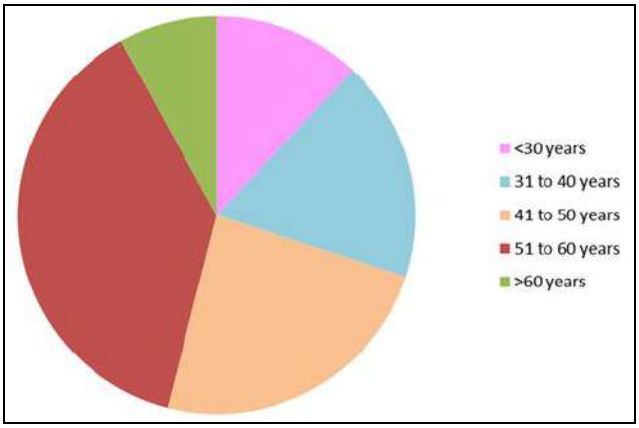


Fig 1: Pie diagram showing age distribution of subjects

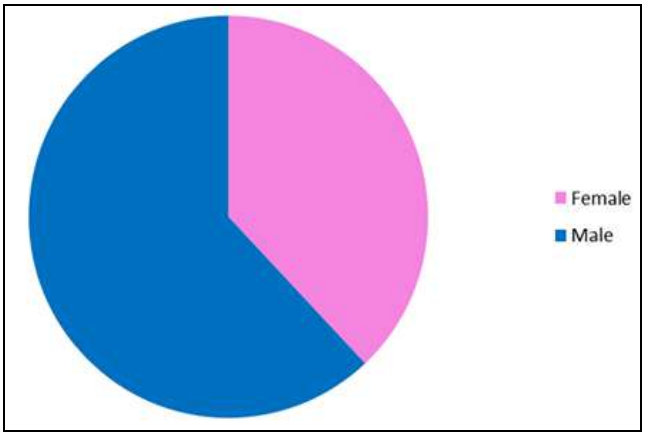


Fig 2: Pie diagram showing sex distribution of the study population.

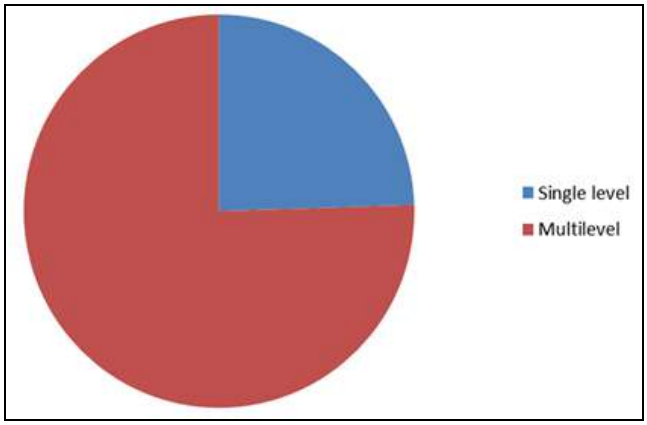


Fig 3: Pie diagram showing the distribution of subjects with single and multiple levels of canal space stenosis

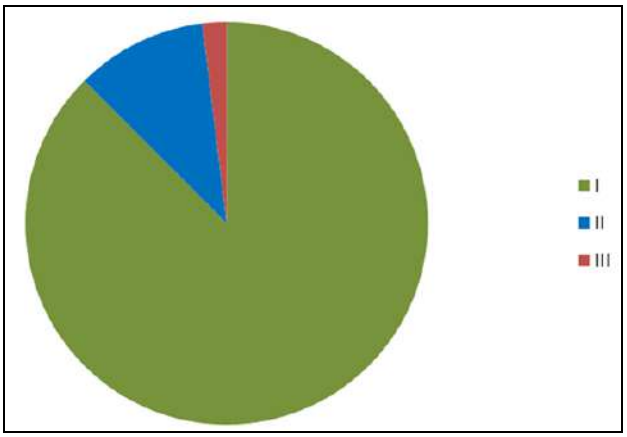


Fig 4: Pie diagram showing grade of stenosis

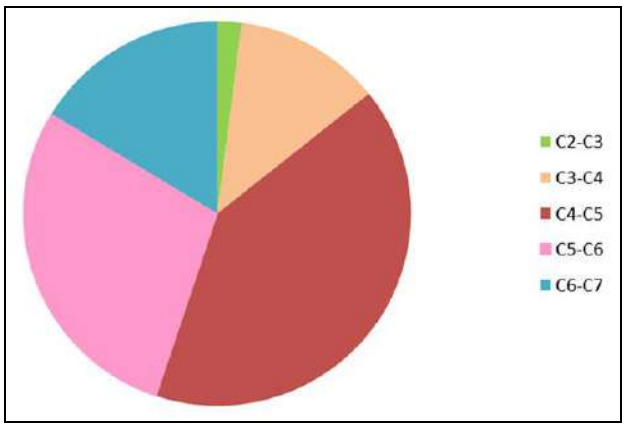


Fig 5: Pie diagram showing distribution of most stenotic level

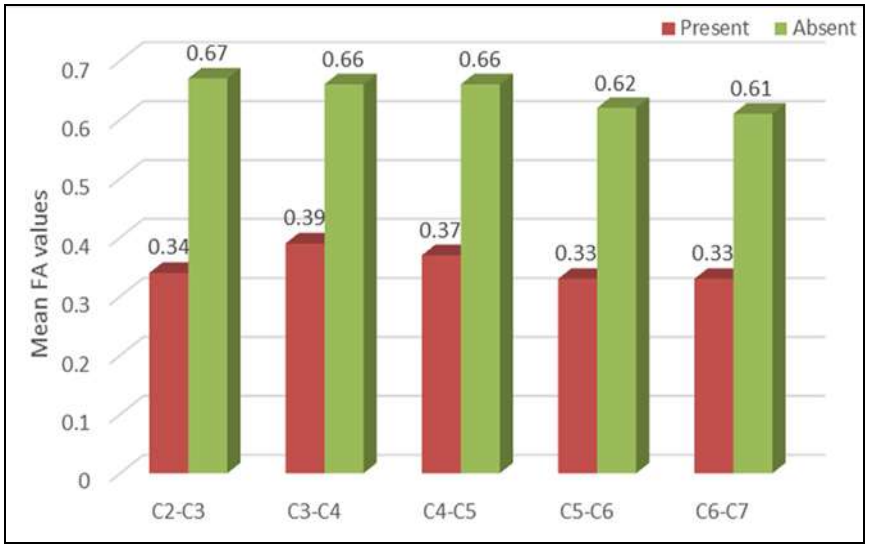


Fig 6: Multiple bar chart showing mean FA at stenotic and non- stenotic segment at each intervertebral level.

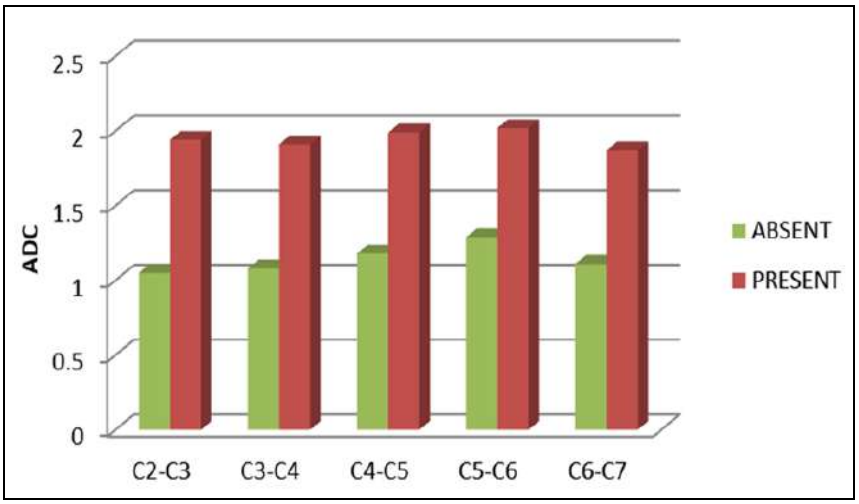


Fig 7: Multiple bar chart showing mean ADC at stenotic and non- stenotic segment at each intervertebral level.

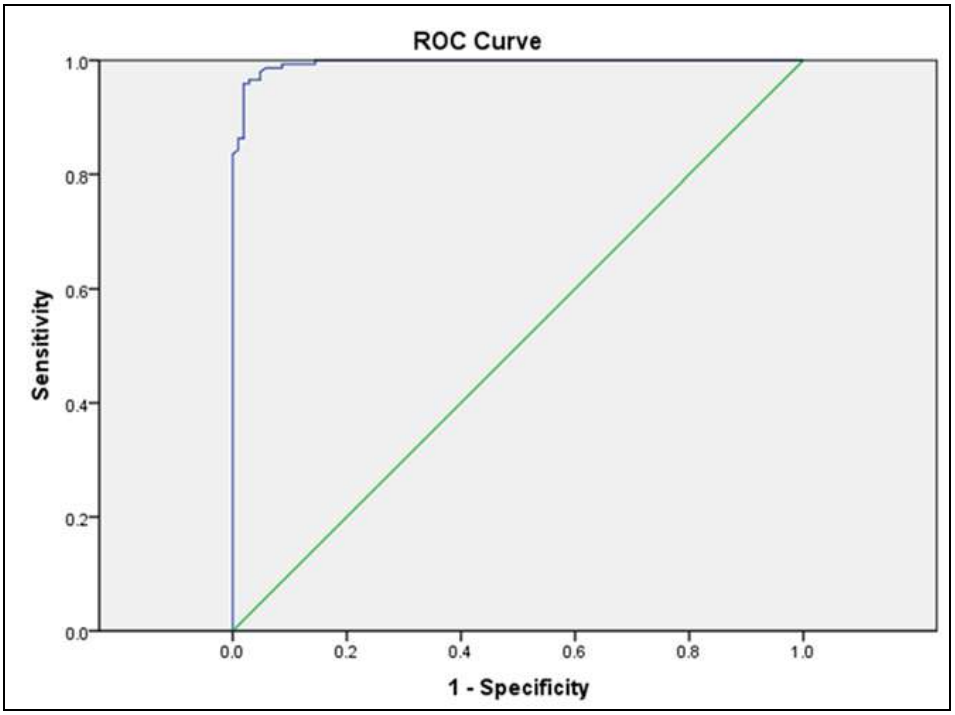


Fig 8: ROC Curve showing the validity of FA in diagnosis of compressive myelopathy.

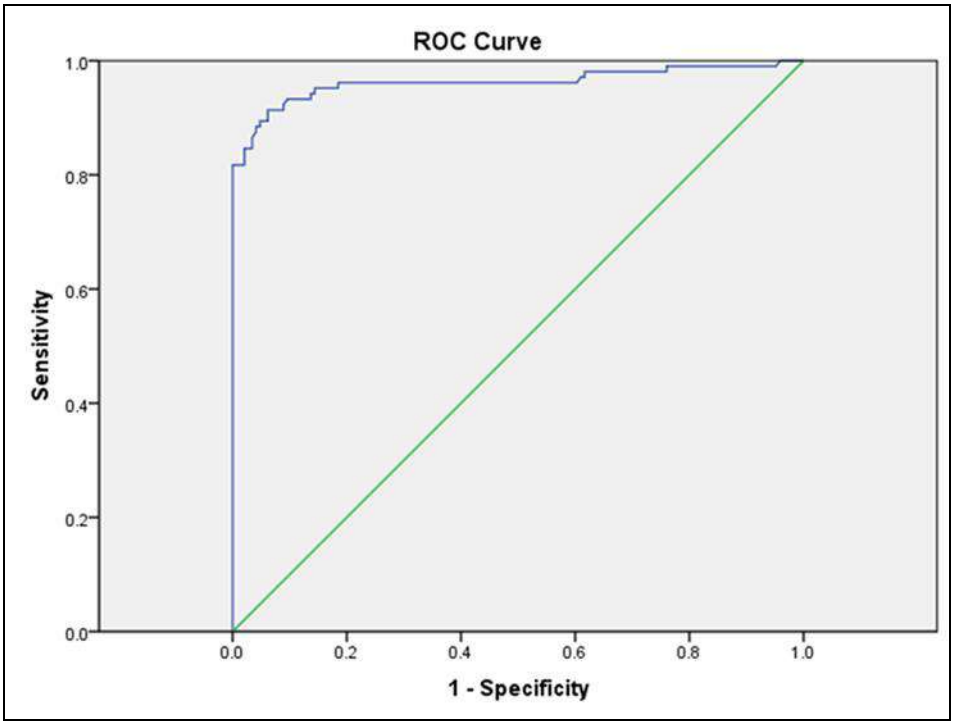
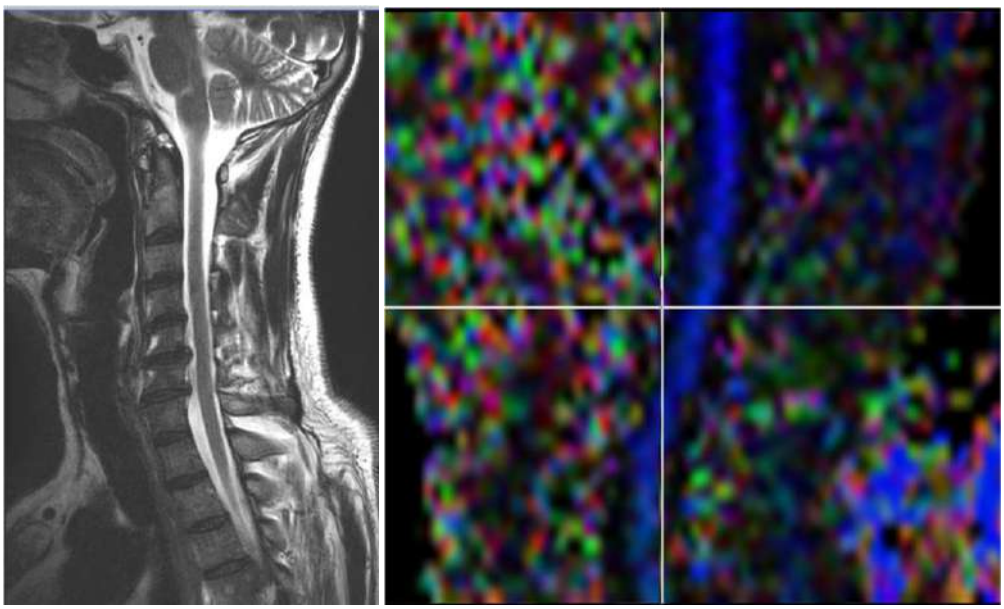


Fig 9: ROC Curve showing the validity of ADC in diagnosis of compressive myelopathy

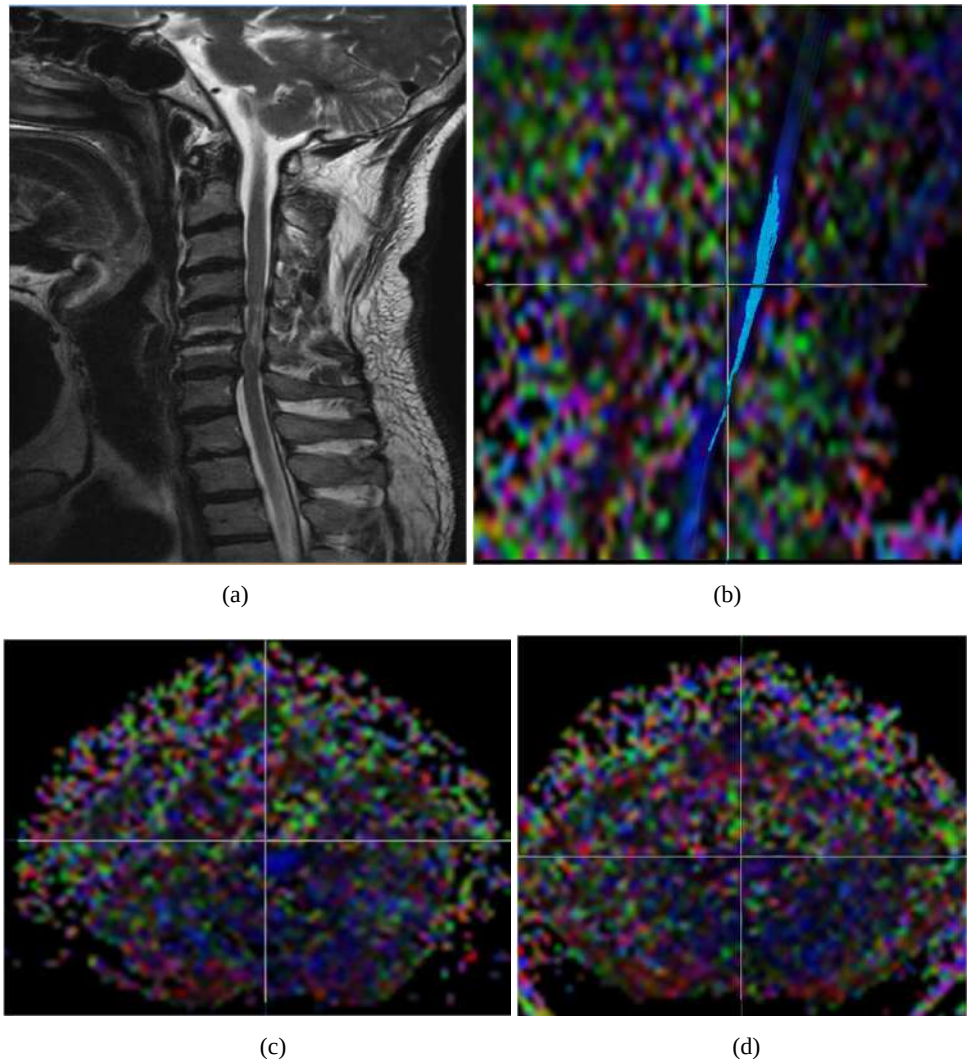


(a) (b)

	Name	Voxels	FA	ADC [10-3mm2/s]
√	ROI 01	2	0.854±0.130	0.648±0.259
√	ROI 02	2	0.803±0.156	0.628±0.220
√	ROI 03	2	0.162±0.004	2.715±0.303
√	ROI 04	2	0.235±0.102	2.585±0.725
√	ROI 05	2	0.425±0.044	1.834±0.410

(c)

Fig 10: (a) Sagittal T2W image showing grade I compression at C4-C5, C5-C6 and C6-C7 intervertebral disc levels. (b) Sagittal DTI images obtained using Philips Fibretrak software. (c) FA and ADC parameters obtained using ROI technique for cervical intervertebral disc levels from C2-C3 to C6-C7 showing low FA and high ADC values at C4-C5, C5-C6 and C6-C7 intervertebral disc levels.



(a) (b)

(c) (d)

Fig 11: (a) Sagittal T2W image showing grade II compression at C6-C7 and grade III compression at C4-C5 and C5-C6 intervertebral disc levels with increased cord signal changes at C4-C5 and C5-C6 levels indicating myelopathy. (b) Sagittal DTI images with single ROI fibre tracking obtained using Philips Fibretrak software demonstrates thinning of the fibres at the C4-C5 and C5-C6 levels. (c): Axial DTI images obtained at the level of C3-C4 show normal cord thickness. (d): Axial DTI images obtained at the level of C5-C6 show relative thinning of the cord.

5. Conclusion

In conclusion, there is significant decrease in the values of fractional anisotropy at the levels with canal stenosis even with normal cord signal intensity. The cut-off value for diagnosing cervical spondylotic myelopathy was FA value ≤ 0.4590 (sensitivity of 100% and specificity of 85.6%). Similarly, there is a significant increase in the apparent diffusion coefficient value at the stenotic levels. The cut-off value was ADC at ≥1.3265 x 10^{-3} mm^2/s (sensitivity of 96.2% and specificity of 76%). Hence the authors recommend the incorporation of DTI in routine MRI assessment of spondylotic myelopathy along with the conventional sequences to help guide the management before irreversible changes set in. However, DTI cannot grade the severity of canal space stenosis and resultant compressive myelopathy.

Potential limitations of the study include a relatively small sample size and a lack of follow-up examinations. Follow up examinations in patients who haven't undergone any surgical or conservative management would help to ascertain and assess the eventual development of cord signal changes on conventional MRI in the segments that DTI had ascertained to have early changes of myelopathy. In addition to this, follow up of patients who have undergone conservative management could impart valuable information regarding the early diagnosis and efficacy of non-surgical conservative therapeutic methods in managing cervical spondylotic myelopathy.

6. References

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