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Original Article

Role of Magnetic Resonance Diffusion Imaging and Apparent Diffusion Coefficient Values in the Evaluation of Extradural Spinal Pathologies

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Abstract

Background: In this study, besides, routine imaging additional diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences were applied to extradural pathologies of the spine to increase the diagnostic confidence in differentiating malignant and benign pathologies.

Aims: The aims are as follows: (a) To differentiate malignancy from infection qualitatively on the basis of DWI sequence and quantitatively on the basis of ADC values. (b) To assign ADC values for infectious/inflammatory pathologies of the spine.

Materials and Methods: This is a prospective study of 53 patients who presented to the department of radiodiagnosis for magnetic resonance imaging spine with extradural spinal pathology. Patients were assessed on 3 Tesla MR SIEMENS LTD.

Results: Mean ADC value in abnormal soft tissue was found to be significantly lower in malignant lesion compared to benign ($P < 0.0001$). Mean ADC value in the affected vertebral body (bone) was found to be significantly lower in malignant lesion compared to benign ($P < 0.0001$). Diagnostic significance of mean ADC value in the affected vertebral body (bone) was assessed using receiver operating characteristic curve. The area under the curve was found to be 95%, and the diagnostic cutoff for the malignant condition was found to be 1.065 (<1.065 malignant) with sensitivity 100% and specificity 83.3%. Diagnostic significance of mean ADC value in abnormal soft tissue showed the area under the curve was found to be 97.4%, and the diagnostic cutoff for the malignant condition was found to be 1.28 (<1.28 malignant) with sensitivity 100% and specificity 93.3%.

Conclusion: In the present study, vertebral bone-marrow pathologies were differentiated as benign or malignant with high sensitivity and specificity with the aid of ADC values calculated from maps obtained by DWI. We conclude that the evaluation of pre/paravertebral soft tissue component should be done to increase the sensitivity and specificity for lesion characterization.

Key words: Apparent diffusion coefficient, Diffusion-weighted magnetic resonance imaging, Vertebral lesions

INTRODUCTION

Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) have recently appeared as a new method of screening in characterizing lesions without necessitating contrast material and in evaluating the vertebrae quantitatively.[1-3]

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ADC is a quantitative parameter calculated from DWI that combines the effects of capillary perfusion and water diffusion.[4] Previous studies have been able to differentiate acute benign compression fractures from malignant compression fractures according to ADC values.[5-10] In a comparatively small number of surveys, ADC values have been studied in discriminating the infectious lesions from the malignant lesions.[6,11,12]

Hence, the present study was done at our hospital to assess the utility of ADC obtained in DW magnetic resonance imaging (MRI) for the differentiation between benign and malignant vertebral lesions, and to determine the sensitivity and the specificity of these vertebral body lesions according to the optimal ADC value cutoff.

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MATERIALS AND METHODS

This study was done in the Department of Radiodiagnosis, Pt. J.N.M Medical College and Dr. B.R.A.M. Hospital, Raipur (C.G), between February 2016 and September 2017 on 53 patients who presented to the Department of Radiodiagnosis. Patients were assessed on 3 Tesla MR SIEMENS LTD.

Prior Institutional Ethical Committee clearance and approval were obtained for the study.

Patients with various extradural spinal pathologies were included in the study, while the patients with spine involvement due to trauma were excluded from the study. All these patients were followed up for confirmation of diagnosis either by bone or soft tissue biopsy/fluid aspirate culture. Informed consent was obtained from the subjects for the inclusion of their images in the study.

Details of clinical history, other related investigations, family history of tuberculosis, anti-tubercular treatment, etc., were taken from all patients before MRI examination. All patients underwent a routine plain MRI of the spine. DW-MRI was also performed in the same sitting in axial images, and at least six ADC values were taken from affected vertebrae and associated soft tissue component.

RESULTS

A hospital study was conducted with 53 patients to assess the role of magnetic resonance diffusion imaging and ADC values in the evaluation of osseous spinal pathologies. The following observations were noted:

- Majority of the patients (41.5%) were in the age group of ≤30 years followed by 51–60 years (20.8%), 31–40 years (18.9%), 41–50 years (15.1%), and >60 years (3.8%).
- There was an almost equal distribution of male (50.9%) and female patients (49.1%) in our study.
- The most common site of involvement was thoracic (56.6%), followed by lumbar (35.8%), sacral (5.7%), and cervical (1.9%).

The radiological findings in our study are summarized in Table 1.

DISCUSSION

DWI is a powerful adjunct to the routine imaging regimen used to detect and characterize extradural lesions. Studies have shown that diffusion is impaired within neoplastic tissue and that a decrease in diffusion coefficient may indicate disease progression.[13]

DWI adds sensitivity to the presence of osseous lesions of the spine. Added to the routine sequences employed for the assessment of suspected metastatic disease and myeloma, DWI improves the detectability and conspicuity of many lesions.[14] In recently presented trials,[15,16] approximately 50% of lesions, identified as part of a neoplastic MRI spine survey, were most conspicuous on trace weighted DWI compared to a combination of routine sequences including sequences and short tau inversion recovery (STIR) and T1 pre- and post-contrast techniques. While approximately 20% of lesions were better seen on routine sequences, up to 10% of lesions were seen only on DWI or were solely evident in retrospect with routine scanning techniques. However, in our study, all the cases were consistent on both routine imaging and DWI.

In the present study, the majority of the patients (41.5%) were in the age group of ≤30 years, followed by 51–60 years (20.8%), 31–40 years (18.9%), 41–50 years (15.1%), and >60 years (3.8%). There was an almost equal distribution of male (50.9%) and female patients (49.1%) in our study.

According to Wahab-Abo-Dewana *et al.* study assessing the utility of ADC obtained in DW-MRI for the differentiation between benign and malignant vertebral lesions found 50 patients 31 males and 19 females, with mean age of 58.45 years and the age ranged from 22 to 87 years presenting with vertebral collapse in one or more vertebral body on conventional MR sequences.[17]

The most common site of involvement in this study was thoracic (56.6%), followed by lumbar (35.8%), sacral (5.7%), and cervical (1.9%).

It was observed in the present study that in 19 (35.8%) cases 2 vertebral bodies were involved while in 11 (20.8%) cases 3 vertebral bodies were involved. 1 and 4 vertebral bodies each were involved for 9 (17%) patients while in 4 (7.5%) and 1 (1.9%) cases 5 and 6 vertebral bodies, respectively, were involved. Benign lesions usually had contiguous vertebral body involvement while the malignant lesions were observed to have non-contiguous involvement.

According to Wahab-Abo-Dewana *et al.* study, L1 was the most commonly fractured vertebra (23 fractures, 23.96%) followed by T12 (20 fractures, 18.4%).[17]

Turna *et al.* in a study on the evaluation of vertebral bone marrow with diffusion-weighted MRI and ADC measurements observed similar findings in their study.[18]

It was observed in the present study that the mean ADC value in the unaffected vertebral body was 0.28 ± 0.01 while

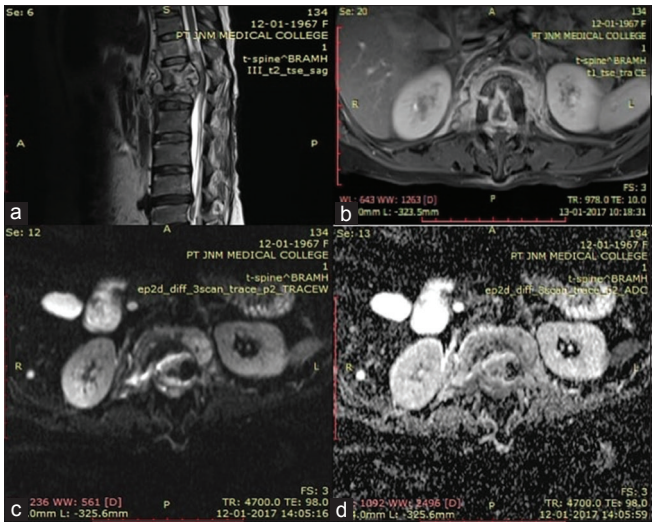


Figure 1: A 50-year-old female presented with bilateral paraplegia (a) sagittal T2-weighted imaging shows heterogeneous hyperintensity with collapse and associated paravertebral and epidural soft tissue component at T12 and L1 vertebrae. (b) Axial T1-weighted post contrast at the level of T12 and L1 vertebrae shows heterogeneous and peripheral enhancement. (c) Axial diffusion-weighted image at same level shows diffusion restriction in the vertebral body and soft tissue. (d) Corresponding axial apparent diffusion coefficient (ADC) map (b = 0 and 1000 s/mm^2 shows decreased signal intensity with an ADC value of 1.26 in bone and 1.55 in soft tissue component). [*On culture, Mycobacterium tuberculosis was grown*]

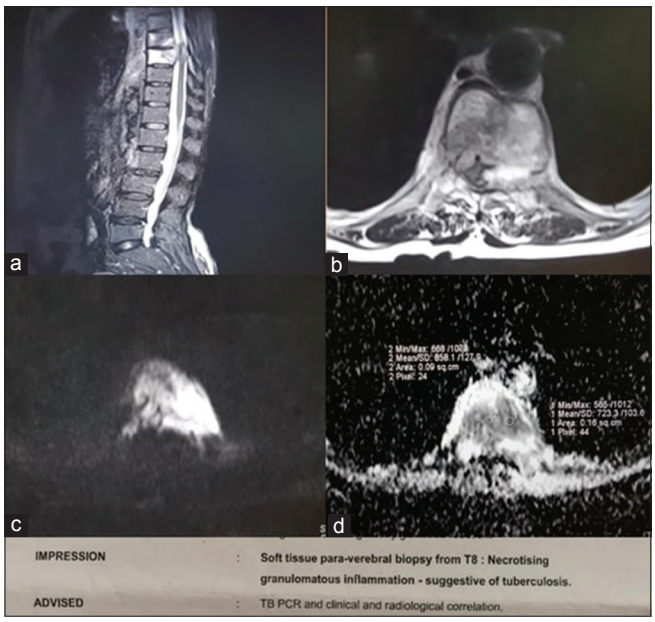


Figure 2: A 61-year-old female presented with bilateral paraplegia. (a) Sagittal T2-weighted imaging (WI) shows heterogenous hyperintensity in T8/9 vertebrae. (b) Axial T2 WI at the level of T9 vertebrae shows expansion with increased signal intensity with the involvement of posterior elements and cord compression. (c) Axial diffusion-weighted image at same level shows diffusion restriction. (d) Corresponding axial apparent diffusion coefficient (ADC) map (b = 0 and 1000 s/mm^2 shows decreased signal intensity with an ADC value of 0.0.79 in bone and 0.94 in soft tissue component). [*Biopsy revealed granulomatous inflammation suggestive of tuberculosis*]

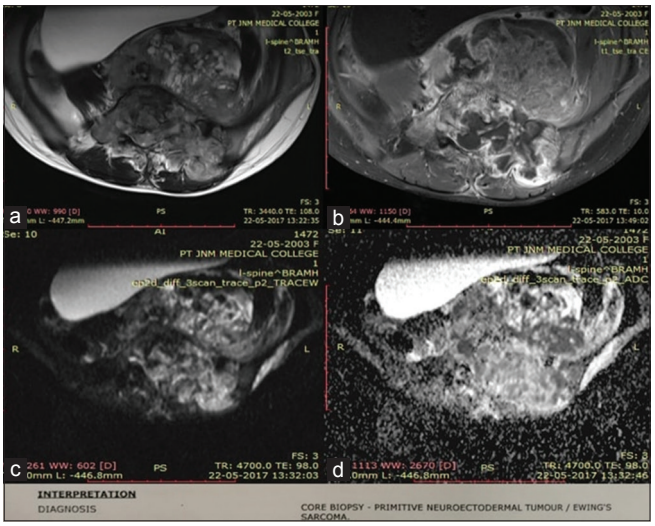


Figure 3: A 14-year-female presented with a large soft tissue mass over the lower back. (a) Axial T2-weighted imaging (WI) shows heterogeneously hyperintensity of L5 vertebrae with associated large soft tissue component. (b) Axial T1-weighted post-contrast image at the level of L5 vertebrae shows heterogeneously enhancement with the involvement of posterior elements and a large paravertebral soft tissue component. (c) Axial diffusion WI at same level shows diffusion restriction in vertebrae and surrounding soft tissue. (d) Corresponding axial apparent diffusion coefficient (ADC) map (b = 0 and 1000 s/mm^2 shows decreased signal intensity with an ADC value of 0.65 in bone and 0.67 in soft tissue component).[Biopsy revealed PNET/Ewing's sarcoma]

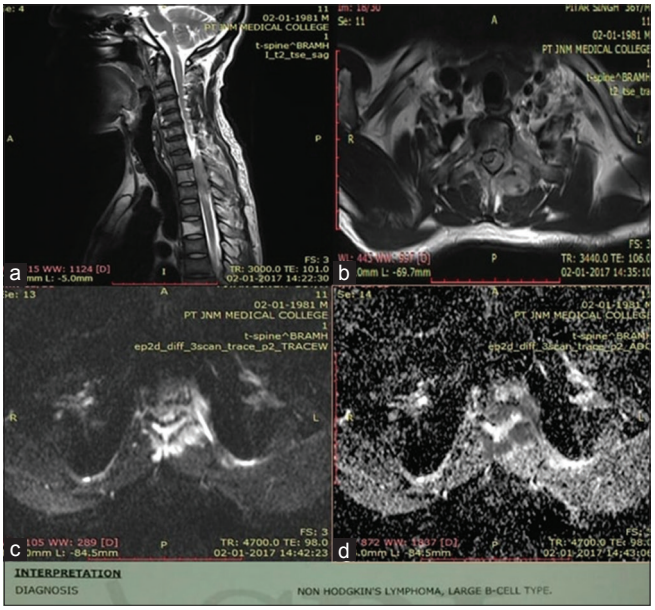


Figure 4: A 36-year-old man presented with quadriparesis. (a) Sagittal T2-weighted imaging (WI) shows heterogeneous hyperintensity of T2 vertebrae. (b) Axial T2 WI at the level of T2 vertebrae shows heterogeneous hyperintensity with the involvement of posterior elements and cord compression. (c) Axial diffusion WI at same level shows diffusion restriction. (d) Corresponding axial apparent diffusion coefficient (ADC) map (b = 0 and 1000 s/mm^2 shows decreased signal intensity with an ADC value of 0.75 in bone and 0.62 in soft tissue component). [*Biopsy revealed large B-cell type Non-Hodgkin lymphoma*]

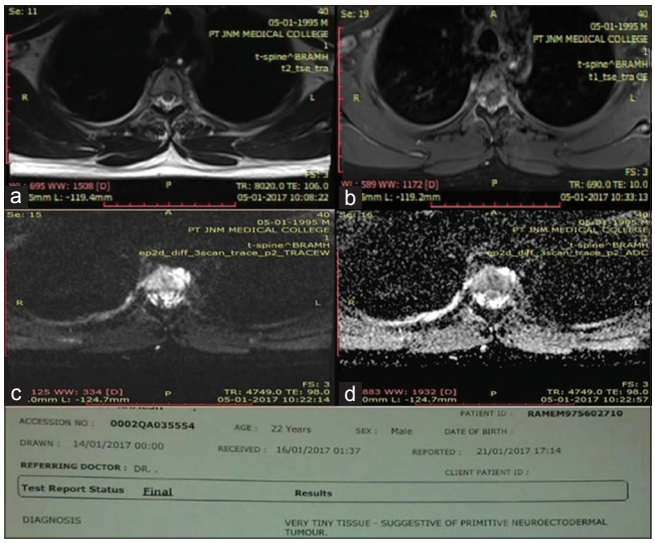


Figure 5: A 22-year-old man presented with bilateral paraplegia. (a) Axial T2-weighted imaging (WI) shows heterogeneous hyperintensity of T5 vertebrae. (b) Axial T1-weighted post-contrast at the level of T5 vertebrae shows heterogeneously enhancement with the involvement of posterior elements and cord compression. (c) Axial diffusion WI at same level shows diffusion restriction. (d) Corresponding axial apparent diffusion coefficient (ADC) map (b = 0 and 1000 s/mm^2 shows decreased signal intensity with an ADC value of 1.05 in bone). [*Biopsy revealed PNET*]

the mean ADC value in the affected vertebral body (bone) was 1.09 ± 0.30. The mean ADC value of abnormal soft tissue component was 1.36 ± 0.54. The most common tissue analyzed in our study subjects was fluid aspirate (49.1%), followed by bone (35.8%) and soft tissue (7.6%).

The histopathology/culture findings in our study showed tuberculous etiology in 49.1% cases while neoplastic etiology in 37.7% cases, respectively. 13.2% of cases showed granulomatous inflammation. The final diagnosis showed 33 (62.3%) cases was benign while 20 (37.7%) cases were malignant.

Diagnostic significance of mean ADC value in the affected vertebral body (bone) was assessed using receiver operating characteristic (ROC) curve in our study. The area under the curve was found to be 95%, and the diagnostic cutoff for the malignant condition was found to be 1.065 (<1.065 malignant) with sensitivity 100% and specificity 83.3% (Table 4).

Wahab-Abo-Dewana *et al.* study reported that mean ADC value of fractured vertebrae was 1.65 ± 0.59 ×10^{-3} mm^2/s. Statistically, significant difference was found between the mean ADC value of normal and fractured vertebrae (P = 0.0001 and P < 0.05).[17]

Diagnostic significance of mean ADC value in abnormal soft tissue was assessed using ROC curve in our study. The area under the curve was found to be 97.4%, and the diagnostic cutoff for the malignant condition was found to be 1.28 (<1.28 malignant) with sensitivity 100% and specificity 93.3%. Diagnostic significance of mean ADC value in the unaffected vertebral body was assessed using ROC curve. The area under the curve was found to be 61.4%, and the diagnostic cutoff for the malignant condition was found to be 0.285 (>0.285 malignant) with sensitivity 57.9% and specificity 69.8% (Grph 2 and Table 4).

Comparison of mean ADC value in unaffected vertebral body between benign and malignant lesions was found to be higher in malignant tissue, but the difference failed to reach statistical significance (P = 0.443). Mean ADC value in the affected vertebral body (bone) was found to be significantly lower in malignant lesion compared to benign (P < 0.0001). Mean ADC value in abnormal soft tissue was found to be significantly lower in malignant lesion compared to benign (P < 0.0001) (Table 3).

Wahab-Abo-Dewana *et al.* study reported that the mean ADC value of the 33 acute benign compression fractures was 1.98 ± 0.44 × 10^{-3} mm^2/s. The mean ADC value of the 22 spondylodiscitis lesions was 1.52 ± 0.14 × 10^{-3} mm^2/s. The mean ADC value of the 31 metastatic lesions was 0.71 ± 0.21 × 10^{-3} mm^2/s. The mean ADC value of the 10 malignant compression fractures was 0.82 ± 0.31 × 10^{-3} mm^2/s. The mean ADC values of the acute benign compression fractures and pyogenic spondylodiscitis were significantly higher than that of the malignant compression fractures (P = 0.0001, 0.007; respectively). The mean ADC value of tuberculous spondylodiscitis was 0.91 ± 0.38 × 10^{-3} mm^2/s, with an overlap with the mean ADC value of malignant CFs (0.75 ± 0.23 × 10^{-3} mm^2/s), and there was a statistically non-significant difference (P = 0.143, P > 0.05) (Figures 1-5 and Table 2). There was a statistically significant difference between all benign CFs and malignant ones (P = 0.002, P < 0.05) (Graph 1).

Balliu *et al.*[6] study on the diagnostic value of ADC to differentiate benign from malignant vertebral bone marrow lesions reported that acute malignant fractures were hyperintense compared to normal vertebral bodies on the DW sequence, except in one patient with sclerotic metastases. Mean ADC value from benign edema (1.9 ± 0.39 × 10^{-3} mm^2/s) was significantly (P < 0.0001) higher than untreated metastatic lesions (0.9 ± 1.3 × 10^{-3} mm^2/s). Mean bone ADC value of infectious spondylitis (0.96 ± 0.49 × 10^{-3} mm^2/s) was not statistically (P > 0.05) different from untreated metastatic lesions. ADC value was low (0.75 × 10^{-3} mm^2/s) in one case of subacute benign fracture.

Biffar *et al.* study on combined DW and dynamic

Table 1: Radiological findings in study subjects

Characteristics	Frequency (%)
MRI T1W sequence	
Hypointense	53 (100)
MRI T2W sequence	
Hyperintense	53 (100)
MRI stir sequence	
Hyperintense	53 (100)
Soft tissue	
Absent	7 (13.2)
Present	46 (86.8)
Enhancement pattern of vertebrae	
Diffuse	21 (39.6)
Heterogeneous	32 (60.4)
Enhancement pattern of soft tissue	
Diffuse	18 (39.1)
Peripheral	28 (60.9)
Cord edema	
Absent	4 (7.5)
Present	49 (92.5)
Intervertebral disc involvement	
Absent	19 (35.8)
Present	34 (64.2)
Posterior element	
Absent	24 (45.3)
Present	29 (54.7)
DWI	
Hyperintense	53 (100)
ADC	
Hypointense	53 (100)

MRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging, ADC: Apparent diffusion coefficient

contrast-enhanced imaging of patients with acute osteoporotic vertebral fractures reported that mean perfusion parameters and ADCs were significantly ($P < 0.001$) different in the fractures compared to adjacent normal appearing vertebrae (Ktrans: 7.81 mL/100 mL/min vs. 14.61 mL/100 mL/min, extracellular volume [ECV]: 52.84mL/100mLvs.4.61mL/100mL,ADC:1.71×10^{-3}mm^2/s vs. 0.57 × 10^{-3} mm^2/s). ADCs showed a significant correlation with the ECV.[1]

In this study, diagnostic significance of mean ADC value in the affected vertebral body (bone) was assessed using ROC curve. The area under the curve was found to be 95%, and the diagnostic cutoff for the malignant condition was found to be 1.065 (<1.065 malignant) with sensitivity 100% and specificity 83.3%. Diagnostic significance of mean ADC value in abnormal soft tissue was assessed using ROC curve. The area under the curve was found to be 97.4%, and the diagnostic cutoff for the malignant condition was found to be 1.28 (<1.28 malignant) with sensitivity 100% and specificity 93.3%.

Wahab-Abo-Dewana *et al.* found threshold value for the mean ADC value was 1.21 × 10^{-3} mm^2/s. Sensitivity, specificity, positive, and negative predictive values were calculated from this threshold value. When

Table 2: Radiological characteristics

Characteristics	N	Mean	SD	SEM	Minimum	Maximum
Mean ADC value in unaffected vertebral body	52	0.28	0.08	0.01	0.12	0.51
Mean ADC value in affected vertebral body (bone)	53	1.09	0.30	0.04	0.61	1.96
Mean ADC value in abnormal soft tissue	46	1.36	0.54	0.08	0.48	2.28

ADC: Apparent diffusion coefficient, the mean ADC value in unaffected vertebral body was 0.28±0.01 while the mean ADC value in affected vertebral body (bone) was 1.09±0.30. The mean ADC value in abnormal soft tissue was 1.36±0.54

Table 3: Comparison of mean ADC value in abnormal soft tissue and in the affected vertebral body (bony) between benign and malignant lesions

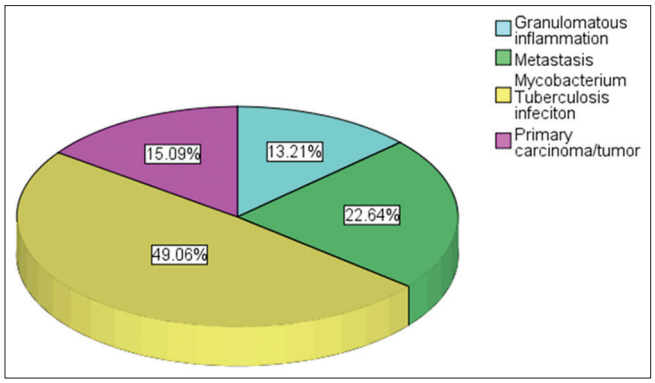
Radiological characteristics	Diagnosis	N	Mean	SD	SE	T	*P* value
Mean ADC value in unaffected vertebral body	Benign	33	0.27	0.09	0.02	−0.77	0.443
	Malignant	19	0.29	0.06	0.01		
Mean ADC value in affected vertebral body (bone)	Benign	33	1.26	0.23	0.04	8.85	<0.0001
	Malignant	20	0.80	0.15	0.03		
Mean ADC value in abnormal soft tissue	Benign	30	1.67	0.35	0.06	9.25	<0.0001
	Malignant	16	0.76	0.23	0.06		

ADC: Apparent diffusion coefficient, Mean ADC value in abnormal soft tissue was found to be significantly lower in malignant lesion compared to benign (*P*<0.0001). Mean ADC value in affected vertebral body (bone) was found to be significantly lower in malignant lesion compared to benign (*P*<0.0001)

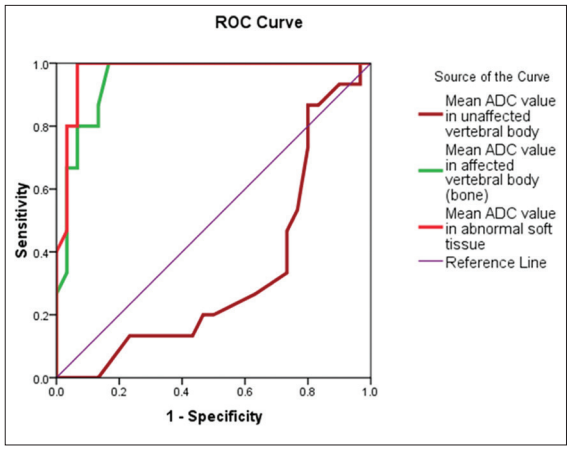
Table 4: Diagnostic significance of various radiological findings

Test result variable (s)	Area under curve	SE	*P* value	Asymptotic 95% CI		Cutoff	Sensitivity (%)	Specificity (%)
				Lower bound	Upper bound			
Mean ADC value in unaffected vertebral body	0.329	0.084	0.064	0.164	0.493	0.335	86.7	20
Mean ADC value in affected vertebral body (bone)	0.950	0.030	<0.0001	0.891	1.009	1.065	100	83.3
Mean ADC value in abnormal soft tissue	0.974	0.021	<0.0001	0.933	1.016	1.28	100	93.3

ADC: Apparent diffusion coefficient



Graph 1: Histopathology/culture findings



Graph 2: Diagonal segments are produced by ties

1.21×10^{-3} mm^2/s was used as the threshold value, the mean ADC values of 4 of the 55 benign lesions were below it, and 2 of the 41 malignant lesions were above it. According to the optimal threshold value of 1.21×10^{-3} mm^2/s set to differentiate vertebral bone marrow lesions as benign or malignant, sensitivity was found to be 95.12%, specificity 92.73%, positive predictive value 90.70%, and negative predictive value 96.23%.[17]

Taskin *et al.*[19] study on value of ADC measurements in the differential diagnosis of vertebral bone marrow lesions stated that according to the optimal cutoff value of 1.32×10^{-3} mm^2/s, determined for the differentiation of benign and malignant vertebral bone-marrow lesions, sensitivity was 96.5%, specificity 95.2%, positive predictive value 96.5%, and negative predictive value 95.2%.

Palle *et al.*[20] study on role of magnetic resonance diffusion imaging and ADC values in the evaluation of spinal tuberculosis found the mean ADC values of 128 vertebral tuberculosis lesions in 56 patients to be 1.4103 mm^2/s and when they took this value as a cutoff in the discrimination of malignant lesions, they found 64.8% sensitivity, 75% specificity, and 74.5% positive predictive values. However, due to the fact that this ADC value displays values overlapping with the ADC values of metastatic vertebral lesions, they emphasized that the ADC values should be evaluated with the clinical history and routine MR findings.

The Limitations of Our Study

The limitations of our study are as follows:

- The imbalance in the age group and sex between the benign and the malignant lesions may have influenced the difference in ADC values.
- Comparisons between low and high field strength machines and their pulse sequences were not taken into consideration while evaluation which may reveal different cutoff values for benign and malignant lesions. Hence, these values cannot be generalized for different scanners from different manufacturers.
- Long-term follow-up of most of the patients who had undergone imaging as a part of our study is not available.

Therefore, we suggest that an understanding of MRI pulse sequences and the normal and age-related appearances of bone marrow is important for the practicing radiologist.

CONCLUSION

In the present study, vertebral bone-marrow pathologies were differentiated as benign or malignant with high sensitivity and specificity with the aid of ADC values calculated from maps obtained by DWI.

ADC values are a useful complementary tool to characterize bone marrow lesions, to distinguish benign infections from malignant bone lesions, particularly for lesions who did not have the classical appearance of either infection or malignancy.

However, there exists a zone of overlap of ADC values in metastatic and infective lesions, which can lead to false negative results. In our study, we suggest use of ADC of paravertebral collection/soft tissue in these cases.

Our study is superior to the previously conducted studies as pre/paravertebral soft tissue component was not evaluated in the previous studies which we strongly recommend to increase the sensitivity and specificity for lesion characterization.

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