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Qualitative and Quantitative Differentiation between Benign and Malignant Vertebral Lesions Using Diffusion Weighted MRI: A Prospective Study

Research Article

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Abstract

Objectives: To differentiate benign from malignant vertebral lesions using Diffusion Weighted MRI Images (DWI) and Apparent Diffusion Coefficient (ADC) values.

Background: In elderly individuals, with no or minimal history of trauma, it is important to diagnose and differentiate benign and malignant lesions affecting the vertebrae. Conventional MRI cannot reliably differentiate benign from malignant vertebral lesions. DWI with ADC is a relatively novel and fast sequence which characterizes lesions based on their cellularity. Our hypothesis is that malignant lesions will show lower ADC values compared to benign by virtue of hypercellularity.

Materials and Methods: A hospital based prospective observational study was conducted with the guidelines of the ethical committee of the hospital. 46 patients with known vertebral lesions and who fulfilled the inclusion criteria were included in this study. Images were acquired on our 3T Philips Ingenia MRI machine and individual ADC values were obtained.

Results: Among 23 benign and 23 malignant vertebral lesions, malignant pathologies showed lower ADC values (0.62 x 10^{-3}mm^2/s) compared to benign lesions (1.08 x 10^{-3}mm^2/s). Cut-off ADC to distinguish benign from malignant lesions was found to be 0.73 ×10^{-3} mm^2/s with a sensitivity and specificity of 95.7% and 82.6% respectively. There was overlap between ADC values for TB (Tuberculosis) and malignancy.

Keywords: ADC; Osteoporosis; TB; Metastases

Introduction

Osteoporosis and osteopenia have affected nearly 50 million people in India and 15-20% of the urban population aged over 50 years show evidence of at least one vertebral fracture [1]. The differential diagnosis for a collapsed vertebra includes trauma, osteoporosis, infections, primary bone tumors, metastasis and multiple myeloma.

In elderly individuals, with no or minimal history of trauma, it is important to diagnose and differentiate benign and malignant lesions affecting the vertebrae. The imaging investigation of choice is conventional MRI which is sensitive but not specific in differentiating among the various possible causes.

In recent years, investigators have studied Diffusion Weighted MRI (DW MRI) and its usefulness in lesions of the spine. Since

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DWMRI depends on cellularity of tissue, it can differentiate an acute benign collapse from metastases as malignant tissues are more cellular and show diffusion restriction.

The quantitative assessment of diffusion in DW MRI is done using Apparent Diffusion Coefficient (ADC). Normal vertebra shows low ADC value due to increased marrow fat which is responsible for water movement restriction. In diseased vertebrae there will be increased ADC values compared to normal vertebra, likely due to increased water content.

In most studies, the ADC value in malignancy was found to be significantly lower than in a benign process, possibly explained by increased cellularity and hence further restricted diffusion.

Most studies however do not standardize the data processing and ROI (region of Interest) calculation on ADC maps. Data on sensitivity and specificity of ADC values in differentiating between infection and malignancy is scarce. Fewer studies have been performed on the diagnostic accuracy of ADC to differentiate tuberculous spondylitis and metastases of the vertebrae, which is a necessity among the Indian patient population.

In our study, we strive to prove the diagnostic accuracy of ADC values in differentiating between benign and malignant lesions of the vertebrae as well as among individual pathologies. We have standardized the ROI in all patients.

Aim

- To Calculate Apparent Diffusion Coefficient (ADC) value for benign vertebral lesions
- To Calculate ADC values for Malignant vertebral lesions
- To assess added value of DWMRI with ADC in the differentiation of benign from malignant vertebral lesions
- To compare ADC values between benign and malignant lesions and to assess its diagnostic accuracy in differentiating between the two groups of lesions
- Whether ADC values can differentiate between infections and malignant vertebral lesions

Materials & Methods

- The study was conducted in the department of Radiology, Jaslok Hospital and Research Centre, on 3T Philips InGenia MRI machine.
- Patients with known benign or malignant lesions of the spine were included in this study. Benign lesions included infection, hemangioma, degenerative spine etc which were diagnosed clinically and on previous imaging, Malignant pathologies were either biopsy proven or had a history of known primary malignancy.
- Patients who were claustrophobic, had metallic implants, and those unwilling to participate were excluded from the study.
- Sample size was 46 and was equally divided into 2 groups, of benign and malignant lesions respectively.
- Standard MR Protocol for Spine was used, with DWI in axial and sagittal planes depending on the lesion. b value of 0 and 400 s/mm^2 was used. **ADC maps were generated and ROI of 55-60mm^2 was drawn on the lesion**. ADC values for individual lesions were noted along with T1, T2 and Diffusion imaging characteristics on excel worksheet.
- Data obtained was analysed using STATA software version 12. Distribution of T1, T2, DWI and ADC scores were compared between the groups using Chi square test or fisher's exact test depending on distribution. ADC scores were compared between benign and malignant groups using unpaired t-test. ROC curve was plotted to find out sensitivity and specificity of ADC Score to determine its diagnostic accuracy.

Results

There were 23 benign and 23 malignant vertebral lesions in this study (Tables 2-5).

DWI restriction was defined as increased signal of the lesion compared to adjacent marrow signal.

Independent t-test was done for testing the hypothesis, which

Table 1: Imaging protocol.

Parameter	Conventional MRI (T1/ T2) Spin echo	DW IMAGING
FOV (mm)	Sagittal : 280-320 Axial: 180-250	Depends on pathology Sagittal : Max 350 Axial : Max 300
Matrix size (Maximum)	512x256	120x80
TR/TE (ms)	T1: 700-1000/10-22 T2: 4000-6000/80-140	4000/55-60
Fat Suppression	Chemical Shift-selective Pulse	Chemical Shift-selective pulse
Section thickness(mm)	Sag: 3 Axial:3-8	3-6
Intersection gap (mm)	0-2	0-2
Turbo factor	T1: 3 T2: 30	
Echo-planar imaging factor	-	55-60
No. of signals acquired	1	2-4

Table 2: Benign lesions (n=23).

Lesion	Frequency	Percentage
Degenerative changes (fatty change)	6	26.2
Hemangioma	4	17.3
Trauma /benign Fracture	4	17.3
Infective discitis (tb)	5 (4)	21.7 (17.3)
Smorl's node	3	13.0
Medullary Infarcts	1	4.4

Table 3: Malignant lesions (N=23).

Lesion	Frequency	Percentage
Metastases	21	91.3
Multiple myeloma	2	8.7

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Table 4: Findings on T1 and T2 images.

	T1		T2		n
	Hyper-intense	Hypo-intense	Hyper-intense	Hypo-intense	
Benign	8	15	11	12	23
Malignant	0	23	7	16	23

Table 5: Association between Dwi and study groups.

		DWI		Total
		No	Yes	
Benign/malignant	Benign	8	15 (65%)	23
	Malignant	1	22 (95%)	23
TOTAL		9	37	46

Table 6: Distribution of Adc between the two groups.

	Benign/ Malignant	N	Mean	Std. Deviation	Std. Error Mean	P value
ADC	Benign	23	1.0813	.38443	.08016	<0.01
	Malignant	23	.6204	.36923	.07699	

Table 7: ROC curve analysis.

Area under the curve				
Area	Std. Error	Asymtomatic sig.	Asymptomatic 95% confidence interval	
			Lower bound	Upper bound
.871	.059	<0.0001	.756	.987

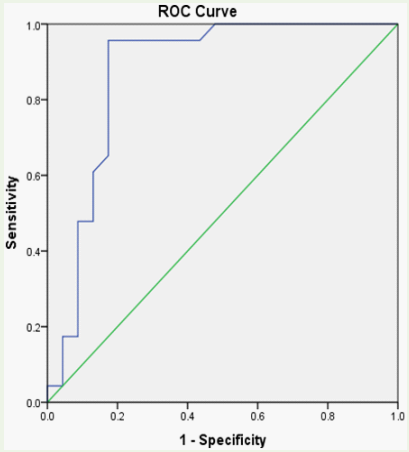

Figure 1: ROC curve analysis.

Table 8: Distribution between ADC values of TB and malignancy.

	TB/ Malignancy	N	Mean	Std. Deviation	Std. Mean error	P value
ADC	TB	4	.9075	.24581	.12291	Could not be calculated
	Malignant	23	.6204	.36923	.07699	

found that ADC scores can be used to distinguish between benign and malignant cases ($p < 0.01$).

The area under the curve was found to be .871 (>0.5), which indicates ADC have a significant association in determining whether lesion is benign or malignant.

The cut-off ADC (x10 13) was found to be ($\times 10^{-3}$ mm^2/s) to distinguish benign from malignant was 0.73 with a sensitivity and specificity of 95.7% and 82.6% respectively.

Since the number of TB cases in our study was only 4, statistically significant comparison between ADC values of TB and malignancy could not be obtained.

Discussion

Diffusion weighted imaging is an MRI technique which can be readily incorporated into routine non contrast MR imaging protocol with little additional scanning time [2]. It offers useful information about the cellularity of the lesion under study.

Spinal DWI is a relatively novel technique to assess vertebral pathologies.

Lesions of the vertebra indicate bone marrow invasion. Normal bone marrow contains significant fat which restricts the movement of water molecules and hence shows diffusion restriction and low ADC value. This is unlike in any other part of the body where the background shows low ADC values. Hence any pathology (Benign or Malignant) which infiltrates the marrow and displaces fat, shows less diffusion restriction and more ADC values than the normal vertebra [3].

Our present study included 46 patients, out of which 23 patients had benign lesions and 23; had malignant lesions of the vertebra.

The most common benign vertebral pathology was degenerative change of the vertebral endplate, followed by infection, trauma and hemangioma.

4 out of 6 patients showed fatty changes or Modic type 2 changes at the vertebral endplate which appeared as widened disc space on fat suppressed DW images. In Modic type 1 change, "claw" of diffusion restriction was seen at the advancing border of proliferative process. This finding is similar to study conducted by K.B Patil et al [4], in which the "claw sign "on DWI was highly suggestive of degeneration while diffuse DWI signal at the endplates with absence of claw sign , was suggestive of infection (Figure 4).

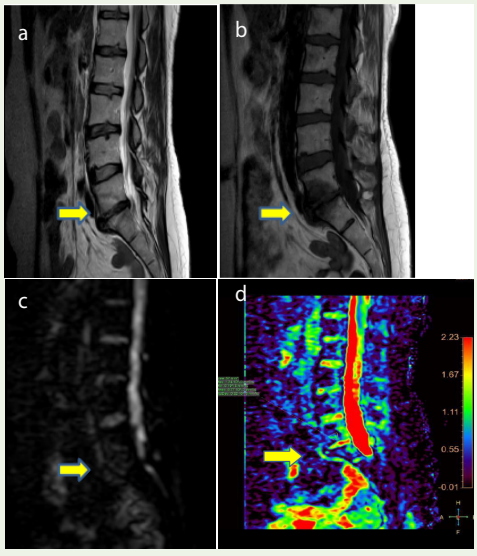

Figure 2: 40 year old study participant with low back pain since 3 months, Sagittal T2 (a) and T1 (b) weighted images of lumbar spine revealed Modic Type 1 changes with characteristic "claw" sign. This endplate lesion showed mild diffusion restriction (c) and ADC values of $0.76 \times 10^{-3} mm/s^2$.

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Among the infections, Tuberculosis (TB) was the most common. ADC values for TB ranged from 0.65 to 1.2 x10^{-3} mm^2/s. There was overlap between ADC values obtained in TB and malignancy. This finding is in accordance with studies conducted by Palle et al and Balliau et al [5,6]. According to Palle et al, false negative results can be obtained when there is dense solid caseation within the vertebrae, and in this situation overlap with ADC values of malignant lesions may be seen. There were only 4 TB cases in our study hence, statistically significant comparison between ADC values of malignancy and TB could not be obtained (Figure 3).

There were 4 cases of post traumatic vertebral fractures in our study. The mean ADC value of these lesions was found to be 1.34 x $10^{-3}mm^2$/s. This high ADC could be attributed to T2 hyperintense edema associated with benign fractures as described in a study by Masayuki et al [7].

The most common benign osseous tumor of the spine is hemangioma. These tumors contain both fat and water and depending on the predominant constituent, exhibit hyperintensity on T1 and T2 weighted images. In a study by Winfield et al [8], the mean ADC value of a typical vertebral hemangioma was found to be 1.085 x 10^{-3} mm^2/s. In our study, the mean ADC among hemangiomas was found to be 0.9 x $10^{-3}mm^2$/s and is higher than that of malignant lesions. This finding is in accordance with most studies where the ADC value of vertebral hemangioma is higher than that of malignant vertebral lesions.

Among the malignant vertebral lesions, most common was metastases. There were 2 cases of multiple myeloma in our study.

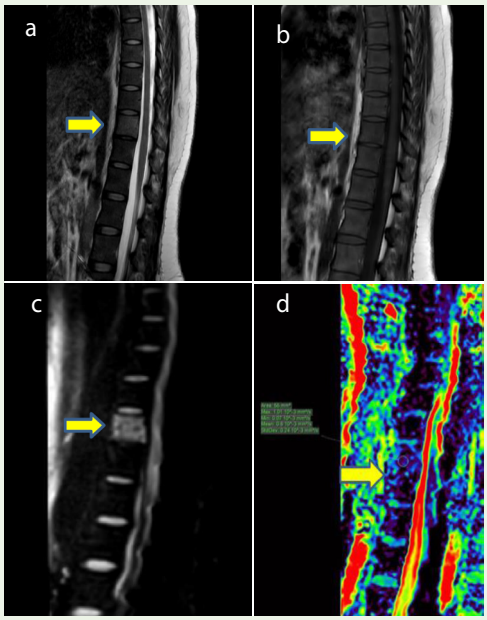

Figure 3: Study participant with known Potts spine, Sagittal T2 weighted image of the dorsal spine revealed diffuse hyperintense signal in D8 vertebral body (a) and Sagittal T1 weighted image showed corresponding iso-hypointensity. On DWI. (c) there was restricted diffusion within the lesion and ADC calculated on color maps (d), was found to be 0.61 x 10^{-3} mm/s^2 .with ROI: 58 mm^2. The low ADC value in this lesion could be attributed to central caseous necrosis.

22 out of 23 malignant and 15 out of 23 benign lesions showed hyperintense signal or diffusion restriction on DWI. Our statistical analysis revealed Positive Predictive Value of 59.4 % and Negative Predictive Value of 88% for malignant lesions.

This finding is in accordance with studies by Baur et al. [9], who found that all but a few cases of metastatic fracture showed hyperintensity relative to normal bone marrow. In fact Bauer et al. found 100% accuracy in the diagnosis of malignant compression fractures using DWI. Although more than 50% benign lesions were hyperintense on DWI, the PPV for this finding was low (40.5%).

In the study by Masayuki Maeda et al [7], qualitative analysis by DWI did not reveal a significant difference between benign and malignant compression fractures. Qualitative analysis has a number of theoretical disadvantages. One problem is that qualitative analysis cannot completely eliminate the T2 shine-through effect. Another problem is that the fraction of fatty marrow in normal vertebrae can vary from patient to patient and vertebrae with a larger fraction of fatty marrow would show DWI hyperintensity.

More promising results have been obtained by the quantitative differentiation of benign and malignant lesions using ADC.

There was a statistically significant difference in ADC values among benign and malignant vertebral lesions in our study. Mean ADC of malignant lesions was found to be lower than that of benign lesions. A cut of 0.73 x 10^{-3} mm^2/s was found with sensitivity of 95.7% and specificity of 85.2 % to distinguish between benign and malignant lesions.

Our findings are in accordance with studies conducted by Dietrrich et al where ADC values of malignant fractures or lesions were typically between 0.7 and 1.3 × 10^{-3} mm^2 /s and that these lesions had lower ADC values compared to benign etiologies [10].

Recent study by Ajit Mahale et al also concluded that the mean ADC of malignant lesions was lower than that of benign. Studies by Shazia Naaz and E Balliu et al also had similar findings [11].

Among malignant lesions in our study, 2 patients had multiple myeloma. The mean ADC of these lesions was 0.49 x$10^{-3}mm^2$/s.

We had three false negative cases of high ADC value among malignant pathologies, one was metastasis from renal cell carcinoma, one from carcinoma lung and from vaginal carcinoma. In these three cases conventional imaging and history were suggestive of pathological collapse, but ADC values were on the higher side (1.83,1.27 and 1.0×10^{-3} mm^2/s). So conventional imaging is a must and DWI should be an add-on sequence (Figure 4).

Ours is the first study to standardize the area of ROI to achieve accurate comparison between ADC values. Despite the false negative cases, the sensitivity of 95.7 % of ADC to distinguish benign vertebral pathologies from malignant pathology is promising.

Conclusion

- ADC for benign vertebral lesions was found to be 1.08 x 10^{-3} mm^2/s

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- ADC for malignant vertebral lesions was found to be 0.62 x 10^{-3} mm^2/s
- **ADC of malignant lesions is lower than that of benign lesions.**
- Hyperintensity on DWI or diffusion restriction was seen in 22 of 23 malignant lesions and had a negative predictive value of 88%.
- There was statistically significant difference in ADC values between benign and malignant vertebral lesions ($p<0.01$).
- The cut-off ADC ($\times 10^{-3}$ mm^2/s) to distinguish benign from malignant was 0.73 with a sensitivity and specificity of 95.7% and 82.6% respectively. Although the cut off values of ADC to differentiate benign and malignant vertebral lesions were different in other studies, our findings are in accordance with the proportionate trend of higher ADC values in benign and lower ADC values for malignant vertebral lesions.
- There was significant overlap between ADC values of TB and malignancy and this result was statistically insignificant.

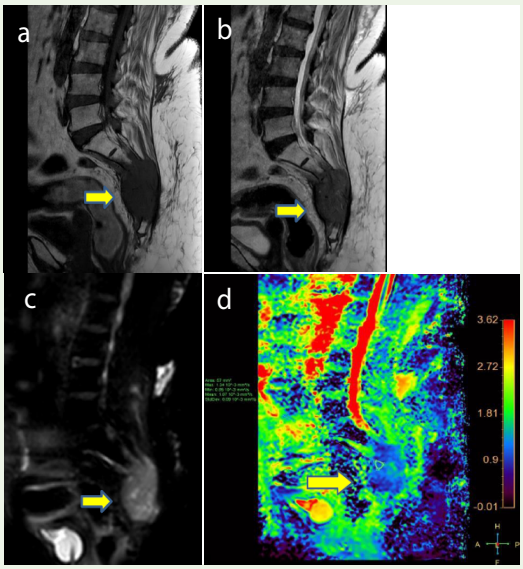

Figure 4: Sagittal T1 (a) and T2 weighted images (b) of lumbosacral spine shows a hypointense metastatic deposit involving S3 and S4 vertebrae. This lesion shows restricted diffusion (c). However ADC values were found to be 1.07 x 10^{-3} mm/s^2. This case formed an exception in our study with high ADC value despite being a malignant vertebral pathology.

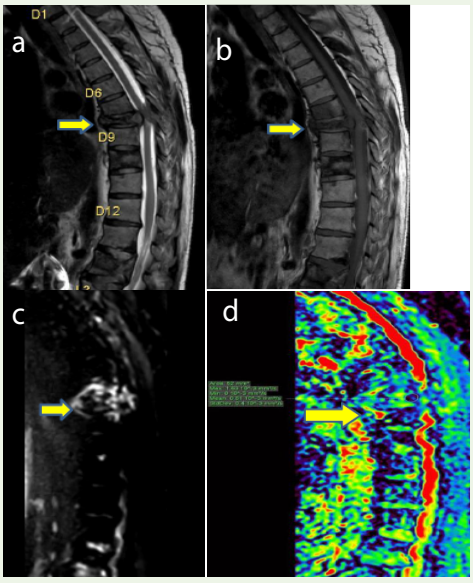

Figure 5: Sagittal T2 weighted image shows vertebral collapse of D8 vertebral body with T2 hypointensity. (a). Corresponding vertebra appears T1 hypointense. (b) There is DWI restriction seen. (c) with ADC values of 0.61 x 10^{-3} mm/s^2. These are metastatic lesions in a known case of carcinoma breast. ADC values are lower than that in benign

Limitation

There were only 4 cases of TB spine in our study, thus statistically significant comparison could not be obtained.

Our study included patients with known malignant lesions of the spine and this represents a selection bias.

Recommendation

DWI is a rapid sequence with very little additional scanning time and should be included in routine imaging of the spine.

ADC should be calculated in all patients with vertebral lesions with standard post processing techniques.

Management of patients with TB and malignancy is different. Hence additional studies to differentiate these entities via imaging are the need of the hour.

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