Section: Miscellaneous

Original Research Article

ROLE OF CHEMICAL SHIFT AND DIFFUSION WEIGHTED MRI IN CHARACTERIZATION OF BENIGN AND MALIGNANT VERTEBRAL BODY LESIONS

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ABSTRAC

Background: Vertebral compression fractures are commonly seen in elderly patients. Benign causes like osteoporotic fractures constitute one third especially in case of a known primary. Metastatic cause should be ruled out particularly in case of known primary. **Objective:** To evaluate the additional role of diffusion and dual phase imaging in investigating vertebral pathologies, in conjunction with routine and standard MRI sequences.
Materials and Methods: This prospective study was conducted among 103 cases. MRI of spine was done. Imaging was performed on a 1.5T MRI GE signa machine. Conventional MRI images were acquired for each patient, followed by standard DWI, dual phase and contrast enhanced images whenever needed.
Results: Most common finding was tuberculosis in 38 cases on histopathology. Benign lesions show no diffusion restriction (mean=1.03 x 10^{-3} mm^2/sec) which is >mean of normal marrow whereas malignant lesion shows diffusion restriction (mean=0.38 x 10^{-3} x mm^2 /sec) which is <adjacent normal marrow. Benign lesions show mean% loss of 42% and malignant lesions 14.35%. Conventional imaging sensitivity=92.96%, specificity=67.3%. Dual phase imaging sensitivity=78.9%, specificity=95.6%. Diffusion weighted imaging sensitivity=96.4%, specificity=69.5%. Threshold value 0.76 × 10−3 mm2/s set to differentiate vertebral bone marrow lesions sensitivity was 85.5%, specificity 66.7%. Addition of dual phase imaging to conventional imaging specificity=95.6%. Addition of diffusion imaging to conventional imaging specificity=86.9%.
Conclusion: Our study demonstrated that diffusion weighted and dual phase imaging can be used as adjunct to conventional MRI for characterizing vertebral lesions as benign and malignant.
Keywords: Magnetic resonance imaging, lesions, benign, malignant.

INTRODUCTION

Vertebral compression fractures are commonly seen in elderly patients. Benign causes like osteoporotic fractures constitute one third especially in case of a known primary. Metastatic cause should be ruled out particularly in case of known primary.[1]
Differentiating benign and malignant causes has clinical significance as it affects the clinical staging and management of the patient. Acute benign osteoporotic collapse of the vertebra due to edema can have signal intensity which is hypointense on T1W, hyperintense on T2W showing post contrast enhancement which is similar to malignant lesions. In this scenario dual phase and diffusion imaging can be used in addition to conventional imaging to characterize the lesion as Conventional MR imaging lacks specificity.
Quantitative diffusion weighted MR imaging by calculating ADC values can be used in conjugation to conventional MR imaging for characterization of the vertebral lesions. Osteoporotic and metastatic lesions can have hyperintense signal on qualitative diffusion weighted imaging, however ADC values of benign lesion will be more than adjacent normal marrow and

of malignant lesion will be less than adjacent normal marrow.[2]

Dual phase imaging is based on presence of fat and water in a single voxel at molecular level. Role of dual phase imaging has been extensively studied in case of adrenal and liver lesions. There are only a few studies in which role of dual phase imaging has been evaluated in case of vertebral lesions. In case of malignant lesions the fat in the marrow is replaced due to tumor infiltration which results in no drop of signal on opposed phase imaging. In contrast benign lesions have fat which leads to signal drop on opposed phase imaging.[3]

The purpose of our study is to evaluate the additional role of diffusion and dual phase imaging in investigating vertebral pathologies, in conjunction with routine and standard MRI sequences.

MATERIALS AND METHODS

Sample size is 103.

Image acquisition and data processing:

MRI of spine was done using following protocol

1) T1 sagittal, axial
2) T2 sagittal, axial
3) STIR sagittal
4) In phase/ opposed phase sagittal
5) DWI sagittal

Imaging was performed on a 1.5T MRI GE signa machine.

Conventional MRI images were acquired for each patient, followed by standard DWI, dual phase and contrast enhanced images whenever needed.

Image analysis

Areas of abnormal marrow signal on T1 / T2 were identified and following conventional MRI imaging features of the lesions are documented and the lesion is characterized as benign and malignant based on following criteria.

Features Favoring Benign

- Intervertebral fluid – fluid levels
- Intervertebral vacuum cleft.
- Degenerative disk disease.

Features Favoring Malignant

- Presence of epidural mass, focal para spinal mass.
- Bulging posterior cortex
- Compression deformity distribution (anterior equivalent to posterior)
- Unilateral / bilateral involvement of pedicle.

In Phase and Out-of- Phase imaging - signal intensity in these areas is calculated on In-phase and Out-of-phase images by drawing ROIs. A cut off of 20percentage is taken. Lesions with cut off > 20% are categorized as benign and percentage loss < 20 % as malignant. DWI- ADC values were calculated in these areas and compared with adjacent normal appearing marrow.

Statistical Analysis

Statistical analysis was performed using SPSS 16 software to obtain the sensitivity and specificity of conventional MR imaging, dual phase and diffusion weighted imaging. Positive predictive value and negative predictive values were calculated. Level of agreement of conventional, dual phase and diffusion weighted sequences with biopsy was calculated by McNamar’s test and dispersion (mean and standard deviation). Kappa analysis was used to attain the agreement between conventional, diffusion weighted imaging and dual phase imaging.

RESULTS

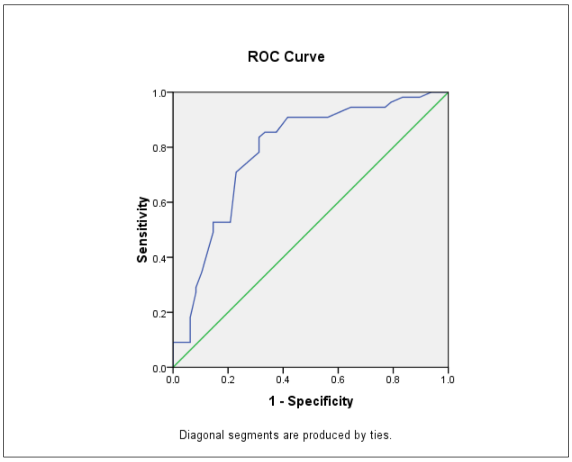

Figure 1: ROC curve

A threshold value was determined, using the ROC, in order to differentiate benign lesions from malignant lesions. According to the optimal threshold value of 0.76 × 10−3 mm2/s set to differentiate vertebral bone marrow lesions sensitivity was found to be 85.5 %, specificity 66.7 %.

Table 1: Histopathology results

Histopathology result	Frequency
Tuberculosis	38
Metastases	22
Multiple myeloma	19
Leukemia	4
Degenerative disease	7
Chronic osteomyelitis	5
Miscellaneous	8

Most common finding was tuberculosis in 38 cases followed by metastases in 22 cases and multiple myeloma in 19 cases. Only four cases had leukemia, seven cases had degenerative disease and five cases had chronic osteomyelitis.

Table 2: Diffusion weighted MR imaging

Results	Mean ADC values	Standard deviation
Normal marrow	0.46	0.27
Benign marrow	1.03	0.04
Malignant marrow	0.38	0.04

Benign lesions show no diffusion restriction with mean of 1.03 x 10^{-3} mm^2/sec. which is greater compared to mean of normal marrow whereas malignant lesion shows diffusion restriction with a mean of 0.38 x 10-3 x mm2 /sec which is less than the adjacent normal marrow.

Table 3: Dual phase imaging –Percentage loss

	Mean (%)	Standard deviation
Benign lesion	42.00	0.26
Malignant lesion	14.35	0.12

Benign lesions show a mean percentage loss of 42% and malignant lesions a mean percentage loss of 14 .35%.

Table 4: Diagnostic accuracy of conventional imaging compared to biopsy

		Biopsy	
		Benign	**Malignant**
Conventional	Benign	53	15
	Malignant	4	31
		57	46
Sensitivity		92.9%	
Specificity		67.3%	
PPV		77.9%	
NPV		88.5 %	

Conventional imaging has high sensitivity of 92.96 % with low specificity of 67.3 % and low positive predictive value of 77.9%.

Table 5: Diagnostic accuracy of dual phase imaging compared to biopsy

		Biopsy	
		Benign	**Malignant**
Dual	Benign	45	2
	Malignant	12	44
		57	46
Sensitivity		78.9 %	
Specificity		95.6 %	
PPV		95.7 %	
NPV		77 .1%	

Dual phase imaging has low sensitivity of 78.9 % with more false negatives results and high specificity of 95.6 % and positive predictive value of 95.7 %.

Table 6: Diagnostic accuracy of diffused weighted imaging compared to biopsy

		Biopsy	
		Benign	**Malignant**
Diffusion Weighted	Benign	55	14
	Malignant	2	32
		57	46
Sensitivity		96.4%	
Specificity		69.5%	
PPV		79.7%	
NPV		94.1%	

Diffusion weighted imaging has high sensitivity of 96.4 %, with low specificity of 69.5 % and low positive predictive value.

Table 7: Comparison using Mc Nemar’s test

Conventional	0.019
Dual	0.01
Diffusion weighted	0.04

Our study proved that dual phase imaging and diffusion weighted imaging has statistically significant adjunct role to conventional imaging for characterization of the vertebral lesions.

Table 8: Measurement of agreement on kappa analysis

	Value	Standard error
Conventional	0.618	0.077
Dual	0.731	0.066
Diffusion weighted	0.678	0.072

Our study showed moderate agreement between conventional, dual and diffusion weighted imaging with biopsy independently with dual phase imaging having stronger agreement with biopsy than diffusion weighted sequence. Comparison is also done by using combination of conventional and dual phase imaging with biopsy and conventional, diffusion weighted imaging with biopsy.

Table 9: Diagnostic accuracy of conventional plus dual phase imaging compared to biopsy

		Biopsy	
Conventional and dual phase		Benign	Malignant
	Benign	45	2
	Malignant	12	44
		57	46
Sensitivity	78.9 %		
Specificity	95.6 %		
PPV	95.7 %		
NPV	77 .1%		

Addition of dual phase imaging to conventional imaging yielded a specificity of 95.6%, positive predictive value of 95.7% and negative predictive value of 77.1%.

Table 10: Diagnostic accuracy of conventional plus DWI imaging compared to biopsy

		Biopsy	
Conventional and DWI imaging		Benign	Malignant
	Benign	53	6
	Malignant	4	40
		57	46
Sensitivity	92.9 %		
Specificity	86.9%		
PPV	89.8%		
NPV	90.9%		

Addition of diffusion imaging to conventional imaging yielded a specificity of 86.9%, positive predictive value of 89.8% and negative predictive value to 90.9%.

Table 11: Comparison using Mc Nemar's test

Conventional and dual phase	0.013
Conventional and diffusion	0.007

Table 12: Comparison using kappa analysis

	Value	Standard error
Conventional and DWI	0.731	0.066
Conventional and DWI	0.803	0.059

Combination of diffusion and conventional imaging has stronger agreement with final biopsy findings than combining dual phase imaging to conventional imaging.

DISCUSSION

Spine being the most common site for metastases, distinguishing benign form malignant etiology is clinically significant. Conventional imaging though can characterize lesion to an extent, there are certain limitations where conventional imaging is not yielding. Newer imaging techniques like dual imaging and diffusion weighted imaging can be used in addition to conventional imaging.

DWI imaging has been used in various clinical settings especially evaluation of cerebral ischemia, demyelination. DWI is known for early detection of ischemic changes than conventional imaging.[3,4] There is growing evidence for diffusion weighted imaging in case of tumor characterization.[5] The role of diffusion imaging in case of spine remains challenging. Malignant lesions appear hyperintense on DWI imaging compared to nonmalignant causes, 5 and by using ADC values malignant lesions will show lower ADC values. Dual phase imaging is based on the principle that marrow infiltration by tumor cells result in replacement of the fat and no loss of signal in out phase imaging, whereas benign lesions show drop of signal.[6-8]

Role of Diffusion weighted imaging in spinal imaging.

Our study included 53 patients with 103 vertebral lesions of which 53 are benign lesions and 46 are malignant. Imaging sequences include sagittal T1W, T2W and STIR and dual phase sagittal, diffusion weighted imaging sagittal with two b values (0 and 700). Post contrast sequences are acquired if required. Qualitative analysis of lesions is done by calculating ADC values by drawing ROI. Largest ROI which fits the lesion is used for calculation of signal intensity. According to our study the mean ADC value for benign lesion is 1.03 x 10-3 mm2/sec, for normal marrow it is 0.46 x 10-3 mm2/sec and for malignant lesions mean is 0.38 x 10-3 mm2/sec with a sensitivity of 96.4% and specificity of 69.5 % with a positive predictive value of 79.7 % and negative predictive value of 94.1%.

Mean ADC values obtained in our study are lower compared to previous studies.

ADC values of malignant vertebral lesions are significantly lower than that of benign lesions, however our study proved that diffusion weighted imaging has low specificity with moderate agreement with biopsy findings.

Initial studies done by Baur et al,[9] on diffusion weighted imaging proved it as a promising tool for differentiating benign and malignant lesions. Both quantitative and qualitative methods were used which include calculation of bone marrow contrast ratio and signal to noise ratio. However the limitation of the study was smaller study group and visual interpretation of the signal intensity changes.

Study by Maeda et al,[10] with 64 patients showed overlap between the ADC values of benign and malignant vertebral body disease however, there is significant difference in the ADC values of benign lesions with a mean ADC of benign vertebral body compression fractures 1.21 ± 0.17 × 10–3 mm2 /s and malignant vertebral compression fractures 0.92 ± 0.20 × 10–3 mm2 /s.

Study was done by Bhugaloo et al,[11] in 35 patients with 68 vertebral lesions and calculated ADC values of the lesions. Both quantitative and qualitative methods by calculating ADC values were done. The study showed though ADC values are nonspecific, normalized lesion to marrow ratio can be used for differentiating benign and malignant lesions with statistically significant difference.

Lalitha Palle et al,[12] conducted a study to assess role of diffusion weighted imaging in spinal tuberculosis. Study included two groups with one group including proven cases of tuberculosis and patients with spinal pathology in second group. The mean ADC value for tubercular lesions obtained in the study is 1.4 +_ 0.2 x 10-3 mm2/sec. The study concluded that quantitative method of diffusion by ADC values can be used for differentiating benign and malignant lesions. However there is overlap of ADC values between malignant and benign lesions especially in case of dense caseating tuberculosis.

Khaled Abdel Wahab Abo Dewan et al,[13] studied 50 patients with 96 vertebral lesions who underwent diffusion weighted MR imaging. The patients were divided into three groups, benign compression fractures, infectious spondylodiscitis and group three malignant compression fractures. The mean ADC value of normal, benign, spondylodiscitis vertebrae was 0.50 ± 0.19, 1.98 ± 0.44, 1.52 ± 0.14 x 10-3 mm2 /s respectively. For malignant lesions the mean ADC value obtained was 0.71 ± 0.21 x 10-3 mm2 /s). By taking cut off value of 1.21 x 10-3 diffusion weighted MRI imaging has a role in differentiate malignant and benign lesions with sensitivity of 95.12%, specificity of 92.73%, positive predictive value of 90.70%, and negative predictive value of 96.23%. Our study concluded that diffusion weighted MR sequence lacks specificity which is in accordance with previous studies.

Role of dual echo imaging

Total of 103 lesions in 53 patients were studied. Signal intensity was measured on in phase, out phase and percentage loss is calculated.

Study done by Erly et al,[14] studied 49 vertebral lesions in 21 patients with h/o primary disease and osteoporotic fractures. Signal intensity ratio was calculated for the lesions. Cut off value of 0.8 with lesions having ratio greater than 0.8 is categorized as malignant and with ratio less than 0.8 as benign. By using 0.8 as cut off the sensitivity is 95 % and specificity is 89% and the study concluded that dual echo imaging has a role in characterization of the vertebral lesions.

D.Z. Zidan et al,[15] conducted study in 32 patients with a known primary malignancy who presented with low back ache with or without history of trauma. Signal intensity ratio was calculated by ratio of signal intensity in opposed phase imaging to signal intensity in T1W imaging. By taking cut off value of 1.2 gave a sensitivity of 88.8, specificity of 80.49 %. The study concluded that out phase imaging in conjugation with conventional T1W imaging can be used to differentiate benign and malignant lesions.

Virna Zampa et al,[16] (2001) conducted study in eight six patients with suspected vertebral lesions. Of these five patients had history of trauma, fifty four had history of malignancy, three patients had clinical symptoms of inflammatory spine disease and rest of them history of back pain with a radiologically suspected compression fractures. Qualitative and quantitative analysis was done. Qualitative assessment includes identifying presence, number of lesions and predicting the nature of the lesion on T1W and opposed phase imaging. Signal intensity ratio was calculated by dividing signal intensity on T1W by signal intensity on opposed phase. A cut off of 1.2 gave a sensitivity, specificity, accuracy, negative predictive value and positive predictive value of 88.8, 80.49, 84.88, 86.4 and 83.33% respectively. Study concluded that opposed phase imaging in addition to T1W imaging can increase the diagnostic accuracy. Our study yielded a mean of 42 % for benign lesions and 14.35 % for malignant lesions. By taking 20 % percentage loss as cut off% sensitivity is 78.9 %, specificity is 95.6%.

Our study concluded that dual phase imaging has low sensitivity with low negative predictive value in identification of benign vertebral lesions and diffusion weighted imaging has low specificity with moderate agreement with biopsy. Our study proved that addition of diffusion weighted, dual phase sequences to conventional imaging increases the specificity. Combination of diffusion weighted sequence to conventional has stronger agreement with biopsy findings than combination of dual phase to conventional imaging.

CONCLUSION

Our study demonstrated that diffusion weighted and dual phase imaging can be used as adjunct to conventional MRI for characterizing vertebral lesions as benign and malignant. Dual phase imaging shows stronger correlation than diffusion weighted imaging when used independently. Using DWI, we have demonstrated that there are clear differences in the diffusion characteristics of Benign and malignant lesions by calculating ADC values which differ. However DWI weighted imaging lacks specificity with high false positive results. Our study proved that addition of diffusion weighted, dual phase sequences to conventional imaging increases the specificity with stronger agreement for diffusion weighted sequence than dual phase sequence.

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