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Original Article

Role of Diffusion-weighted Imaging in Differentiating Benign from Pathological Vertebral Collapse on the Basis of Apparent Diffusion Coefficients Values

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Abstract

Introduction: Vertebral collapse is a common clinical problem. According to the demographic changes in our society, the incidence and prevalence of vertebral collapse are increasing. Vertebral collapse is associated with increased morbidity and mortality. Hence, vertebral collapse has a significant impact on the patient's overall quality of life and on the patient's life expectancy. The causes of vertebral collapse are manifold including benign and malignant causes. The differential diagnosis for a collapsed vertebra includes trauma, osteoporosis, infections, primary bone tumors, metastasis, and multiple myeloma.

Materials and Methods: Sixty-six patients with acute vertebral collapse were imaged using conventional MRI, fat-suppressed contrast-enhanced T1WI, and DWI sequence on a 1.5 T MR machine. Assessment of the abnormal signal intensity was done quantitatively by measuring apparent diffusion coefficients (ADCs). Furthermore, these areas of abnormal signal intensity were compared to adjacent normal marrow.

Results: The study comprised 66 patients, of which 46 cases (69.7%) were benign vertebral collapse and 20 cases (30.3%) were pathological collapse. Mean ADC (±SD × 10^{-3} mm^2/s) in the benign vertebral collapse was 1.4578 ± 0.2992, whereas the mean ADC (±SD × 10^{-3} mm^2/s) in the pathological vertebral collapse was 0.8520 ± 0.1786. We found out that the difference in mean ADC values between benign and pathological vertebral collapse was statistically significant.

Conclusions: DWI-ADC is a reliable adjunct parameter that supports conventional MRI in differentiating benign and malignant vertebral fractures.

Key words: Fractures, Metastasis, Multiple myeloma, Trauma, Vertebral

INTRODUCTION

Vertebral collapse is a common clinical problem. According to the demographic changes in our society, the incidence and prevalence of vertebral collapse are increasing. Vertebral collapse is associated with increased morbidity and mortality. Hence, vertebral collapse has a significant impact on the patient's overall quality of life and on the patient's life expectancy. The causes of vertebral collapse are manifold including benign and malignant causes. The differential diagnosis for a collapsed vertebra includes trauma, osteoporosis, infections, primary bone tumors, metastasis, and multiple myeloma. Osteoporosis is the leading cause of non-traumatic vertebral collapse. By the age of 80, 40% of women and 20% of men can be expected to have suffered osteoporotic spinal fracture. Less frequently seen is vertebral collapse following metastatic, hematologic, or neoplastic conditions. The spine represents the most frequent site of skeletal metastasis predominating in the thoracic and lumbar spine. Vertebral marrow lesions in patients with known primary malignancy are a common clinical problem, particularly in elderly patients. Despite osteoporosis being the most common cause at this age, the spine also is a common site of metastases, with about 39% of all bone metastases occurring in the spine. Such metastases may result in a pathologic fracture. Thus, it is

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essential to differentiate benign from malignant vertebral collapse because their medical management and their outcome are substantially different.

Conventional MRI has good sensitivity but lacks specificity in differentiating acute benign from pathological collapse. MR imaging findings such as abnormal signal intensity of the pedicle or posterior element, an epidural or paraspinal mass, and a convex posterior border of the vertebral body are useful for the differentiation of metastatic from acute osteoporotic compression fractures of the spine. Furthermore, multiple compression fractures, retropulsion of a posterior bone fragment, a low-signal intensity band on T1WI and T2WI, and spared normal bone marrow signal intensity of the vertebral body are suggestive of acute osteoporotic compression fractures. However, this differentiation can be problematic due to edema, hemorrhage, and the presence of repair tissue that accompanies acute benign collapse which results in bone marrow changes which resemble metastatic collapse. Even post-contrast T1WI MRI is also not very helpful because there is disruption of the blood-bone barrier in acute benign collapse leading to post-contrast enhancement. Adding diffusion-weighted imaging (DWI) sequence to routine, conventional MRI sequences are helpful.

DWI is a functional MR imaging sequence that relies on the detection of Brownian motion of free water molecules within voxel of tissue. It is based on the principle that water molecules in a tissue show a different Brownian motion depending on variations in microstructure. Signal attenuation reflects the degree of water motion with a proportional relationship. ADC value allows the quantification of this Brownian motion and is calculated from maps derived by diffusional signal attenuation. Briefly, tissues with high free water components, such as those with lower content of membranes and intracellular organelles or high free extracellular water content, show lower signal intensity on DWI and higher signal intensity on ADC maps in comparison to muscles. Conversely, tissues with restricted extracellular water content, such as those with high cellularity, as tumors, show higher signal intensity on DWI and iso-hypo intensity on ADC maps. Restricted diffusion on DWI shows low ADC value, whereas free diffusion on DWI shows high ADC values. ADC values can also be used to evaluate response to treatment as well as the progression of the disease. Thus, both qualitative as well as quantitative functional information concerning the microscopic movements of water at cellular level can be obtained from DWI. In addition to the characterization of lesions, DWI has also been used as a tumor screening technique for the whole body, such as positron-emission tomography (PET).

Some studies have suggested a significant role of DWI in the assessment of vertebral marrow pathologies, whereas few others have shown only equivocal results. In this prospective study, we evaluated the hypothesis that DWI and ADC values have a role in differentiating benign from pathological vertebral collapse. Hence, we carried out this study in our setup with the purpose of prospectively determining the value of adding qualitative and quantitative axial DW imaging to standard spine MR imaging to differentiate between acute benign and pathological vertebral collapse.[1-6]

MATERIALS AND METHODS

This was a prospective study conducted from January 2020 to October 2021 in GSVM Medical College, Kanpur, India. Approval from the ethical committee was obtained before the study. The study includes 66 patients (33 women and 33 men) in the age groups of 13–79 years who were referred to the Department of Radiodiagnosis with a previous radiograph demonstrating vertebral collapse. Patients who were referred within 4 weeks of the onset of clinical symptoms were selected for the study. Informed consents were obtained from the patients.

The study was carried out on a 1.5T MRI machine using a standardized protocol on a phased-array spinal coil. All the patients will be subjected to conventional MRI sequences in the sagittal plane, which include T1 turbo spin-echo (TSE), T2 TSE, STIR (sagittal/coronal plane) sequences, and post-contrast fat-suppressed T1 as an optional sequence with a thickness (mm) 4 mm, TR/TET2-3500/103; T1-703/11; STIR-3500/78; T1-FS post-contrast-530/11.3800/82 Matrix size 384 × 384 92 × 180 FOV 330 350. DWI was carried out using single-shot echoplanar Imaging (SS-EPI) in a sagittal plane with a minimum of two b-values. The max b-value used was b 800. Sensitizing diffusion gradients were applied sequentially in the x, y, and z directions. ADC maps were generated with the software supplied by the manufacturer on a pixel-by-pixel basis from the DWI. ROI was defined in areas with abnormal signal intensity on max b-value DWI and copied to the ADC map.

In our study, a qualitative assessment was done by comparing diffusion images with ADC maps to look for the presence or absence of diffusion restriction in a collapsed vertebra. Quantitative assessment was done by placing at least two ROI in areas with abnormal signal intensity on max b-value DWI and copying to the ADC map. ROI was also placed in the marrow of normal vertebra to calculate their mean ADC values.

Statistical Analysis

For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed by the SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables—two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. Once a t-value is determined, a p-value can be found using a table of values from the Student's t-distribution. The $P \leq 0.05$ was considered to be statistically significant.

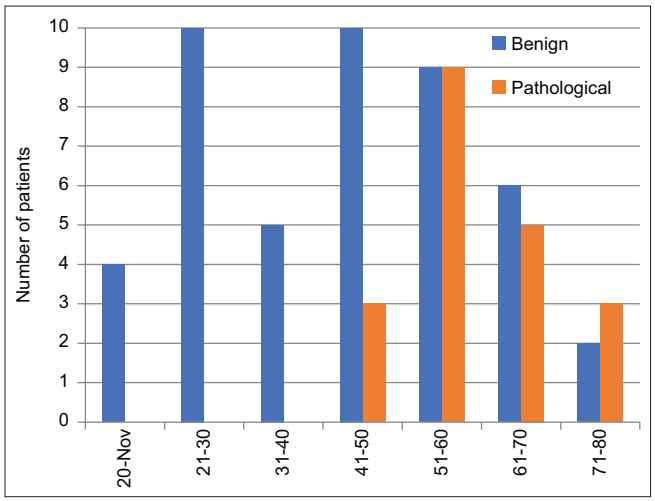

Figure 1: Association between ages in the group

RESULT

The study comprised 66 patients, of which 46 cases (69.7%) were benign vertebral collapse and 20 cases (30.3%) were pathological collapse. In benign collapse, nine cases (19.5%) were due to osteoporotic compression fractures, nine cases (19.5%) were due to acute traumatic collapse, and 28 cases (61.0%) were due to Pott's spine. The mean age for osteoporosis compression fracture was 62 years,

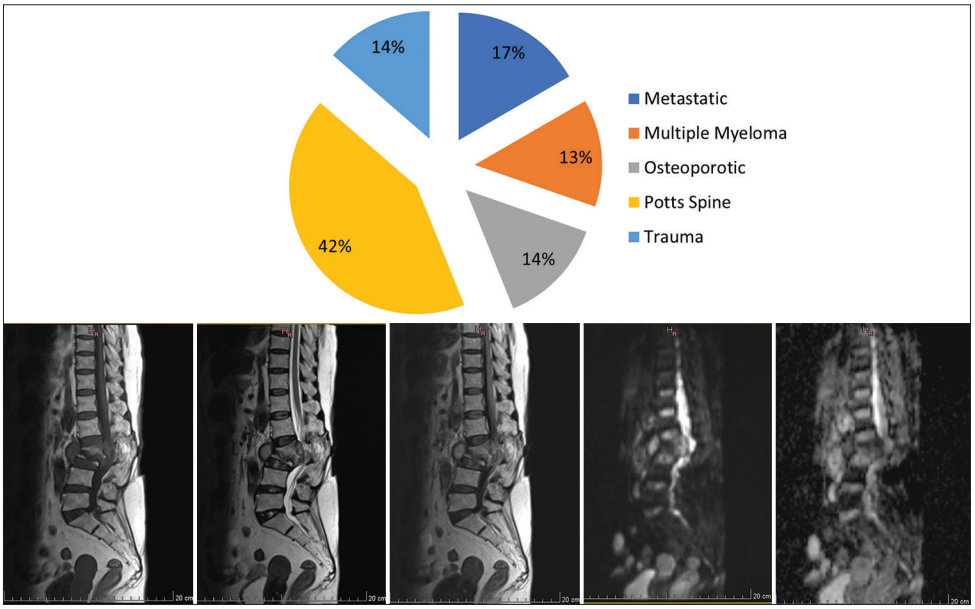

Figure 2: A 62-year-old female patient presented to emergency confirmed as a case of Pott's spine. On T1WI (a), T2WI (b), and STIR (c) showed altered marrow signal intensities seen as patchy and confluent areas of T1/T2 prolongation involving L2 and L3 vertebral bodies with the destruction of endplates and cortical margins. It also shows the partial collapse of the L2 and L3 vertebra. There is the partial destruction of the intervening disc with a reduction of disc space. The lesion shows diffusion restriction on DWI (d). On ADC map (e), ADC at this level is 1.3 × 10^{-3} mm^2/s

Table 1: Distribution of mean ADC-values (×10^{-3} mm^2/s) and ADC-values (×10^{-3} mm^2/s)

	Number	Mean	SD	Minimum	Maximum	Median	*P*-value
ADC-values (×10^{-3} mm^2/s)							
Benign	46	1.4578	0.2992	0.7200	2.1000	1.4600	<0.0001
Pathological	20	0.8520	0.1786	0.6100	1.3100	0.8400	
ADC-values (×10^{-3} mm^2/s)							
Metastatic	11	0.8672	0.1635	0.6700	1.2600	0.8500	0.0009
Multiple myeloma	9	0.8333	0.2039	0.6100	1.3100	0.7900	

ranging from 45 to 75 years. The traumatic group's mean age was 25 years, ranging from 13 to 38 years. The mean age for vertebral collapse due to Pott's spine was 45 years ranging from 23 years to 70 years. Pathological collapse which included nine cases (45.0%) of multiple myeloma and 11 cases (55.0%) of metastatic compression fractures. The mean age in the multiple myeloma group was 60 years ranging from 50 to 71 years, and in the metastasis group was 60 years ranging from 46 to 79 years [Figure 1].

Mean ADC ($\pm$SD$\times 10^{-3}$ mm^2/s) in normal vertebral marrow was $0.326 \pm 0.121 \times 10^{-3}$ mm^2/s, ranging from $0.3–0.67 \times 10^{-3}$ mm^2/s. Mean ADC ($\pm$SD $\times 10^{-3}$ mm^2/s) in the benign collapse was 1.4578 ± 0.2992. Mean ADC ($\pm$SD $\times 10^{-3}$ mm^2/s) in the pathological collapse was 0.8520 ± 0.1786. We found out that the difference in mean ADC values between benign and pathological vertebral collapse was statistically significant; however, within the pathological group, the difference in mean ADC values between multiple myeloma and metastatic vertebral collapse was statistically insignificant ($P > 0.005$) [Table 1 and Figure 2].

DISCUSSION

This was a prospective study conducted from January 2020 to October 2021 in GSVM Medical College, Kanpur, India. Approval from the ethical committee was obtained before the study. Differentiation between malignant and benign vertebral compression fracture is a common problem in the management of the patients: establishing the correct diagnosis is of great importance in determining treatment, surgical approach, and prognosis. Although MR imaging using conventional T1 WI and T2 WI has proved helpful in differentiating between benign and malignant causes of vertebral collapse, confident diagnosis is not always possible.

We conducted our study with a b-value of 800, which gave us reasonable SNR and ADC maps. Although multiple b-values give good SNR and accurate ADC values, scan times are prolonged, any movement during this time period can lead to motion artifacts.

In our study in the benign group, 4 (8.7%) patients were 11–20 years old, 10 (21.7%) patients were 21–30 years old, 5 (10.9%) patients were 31–40 years old, 10 (21.7%) patients were 41–50 years old, 9 (19.6%) patients were 51–60 years old, 6 (13.0%) patients were 61–70 years old, and 2 (4.3%) patient were 71–80 years old. In the pathological group, 3 (15.0%) patients were 41–50 years old, 9 (45.0%) patients were 51–60 years old, 5 (25.0%) patients were 61–70 years old, and 3 (15.0%) patients were 71–80 years old. Hence, we infer that benign vertebral collapse more frequently occurs in the younger age group <50 years, accounting for 63% of patients in the benign group, whereas the malignant vertebral collapse most commonly occurs in the old age group of above 50 years comprising 85% of cases of the malignant group.[7-12]

In our study, benign vertebral collapse showed a mean ADC of $1.4578 \pm 0.2992 \times 10^{-3}$ mm^2/s, and pathological collapse showed a mean ADC of $0.8520 \pm 0.1786 \times 10^{-3}$ mm^2/s. According to Ajith Mahale *et al.*,[13] with b-values of 600 s/mm^2, acute benign collapse showed a mean ADC of $1.466 \pm 0.325 \times 10^{-3}$ mm^2/s, and pathological collapse showed a mean ADC of $0.959 \pm 0.288 \times 10^{-3}$ mm^2/s. Furthermore, according to Arashdeep Kaur *et al.*,[14] the mean ADC value of benign pathologies was $1.66 \pm 0.32 \times 10^{-3}$ mm^2/s and malignant collapse showed a mean ADC of $0.69 \pm 0.15 \times 10^{-3}$ mm^2/s.

Vertebral metastases represent the secondary involvement of the vertebral spine by hematogenously disseminated metastatic cells. In general, these bone marrow vertebral metastases appear on DWI as high-signal intensity areas in an otherwise hypointense vertebral marrow. These areas correspond to low-signal intensities on ADC maps. It is well known that bone metastases can be prevalently lytic or sclerotic. Although in both types of metastases, the bone turnover is more pronounced than in normal bone marrow, in osteolytic metastases, the osteoclastic activity is prevalent as it is stimulated by the adjacent metastatic tumor cells. The osteoblastic metastases origin from the prevalent stimulation of osteoblasts. Osteolytic lesions are better detected on DWI imaging due to the higher content of water and cells with respect to the sclerotic ones.

Multiple myeloma is a primary malignant neoplasm due to abnormal proliferation of plasma B-cells leading to marrow infiltration. Diagnosis requires pathological, biochemical, and radiological evaluation. In multiple myeloma, the marrow cells are replaced by tumor cells which lead to diffusion restriction. ADC values of multiple myeloma are higher than normal bone marrow. MRI and DWI are helpful in assessing the tumoral burden in multiple myeloma. It also has a role in assessing treatment response. Multiple myeloma lesions appear T1 hypointense, T2 hypointense, and STIR hyperintense. In DWI, the lesions appear hyperintense and by calculating ADC values, it is even possible to assess treatment responders from non-responders.

The mean ($\pm$SD) ADC value in multiple myeloma was $0.8333 \pm 0.2039 \times 10^{-3}$ mm^2/s, whereas the mean ADC in metastatic compression fractures was $0.8672 \pm 0.1635 \times 10^{-3}$ mm^2/s. Furthermore, the difference in mean ADC values of both multiple myeloma and metastatic vertebral collapse was not statistically significant. This finding of our

study is seen in accordance with Ajith Mahale *et al.*[13] with b-values of 600 s/mm^2 where mean ADC values in metastatic compression fractures were $0.970 \pm 0.237 \times 10^{-3}$ mm^2/s and mean (±SD) ADC value in multiple myeloma was $0.936 \pm 0.395 \times 10^{-3}$ mm^2/s. With this result, we can conclude that DWI is not helpful in differentiating metastasis and myeloma. Hence, to distinguish metastasis and myeloma, other confirmatory tests should be performed.

Therefore, in our study, we observed that the mean ADC measurement of normal vertebrae was $0.326 \pm 0.121 \times$ 10–3 mm^2/s, and the mean ADC measurement of all the collapsed vertebrae (benign and malignant) was $1.274 \pm 0.3872 \times 10^{-3}$ mm^2/s, which was significantly greater than that of normal ones ($P < 0.0001$), and this finding is indicative of diminished diffusivity of the normal fatty marrow. The tumor cells infiltrate and replace the bone marrow, thus also limiting free water diffusion. Accordingly, we found that the mean ADC measurement of vertebrae with malignant marrow lesions was less than those with benign pathologies. However, the mean ADC value of the vertebrae with malignant marrow pathologies was greater than those with normal fatty marrow. On the other hand, benign acute vertebral fractures have an increased quantity of free water in the interstitial region with an escalation of water diffusion and leading to high ADC values. Furthermore, in our study, we observed that the mean ADC value of benign pathologies ($1.4578 \pm 0.2992 \times 10^{-3}$ mm^2/s) was statistically greater than those of malignant ones ($0.8520 \pm 0.1786 \times 10^{-3}$ mm^2/s) ($P < 0.0001$). Therefore, diffusivity (ADC values) was found to be highest in benign lesions, followed by malignant pathologies, and least in vertebrae with normal fatty marrow. Although the measured ADC may be indicative of benign or malignant lesions, a considerable overlap has been described in several studies. Our outcomes are in agreement with the many previous studies in the literature.

In our experience, according to the literature, we found that DWI and ADC values are very much useful in differentiation between benign and malignant vertebral collapse.

CONCLUSION

DW-MRI of the vertebral marrow is a beneficial sequence that can be used for vertebral collapse. Quantitative ADC values can be useful in differentiating benign from pathological causes of vertebral collapse. The major advantage of this sequence is that no ionizing radiation is administered, and no injection of isotopes or any contrast medium is required. Short data acquisition time is another advantage. Therapy assessment may be done by observing changes in extent, symmetry, and intensity of signal on high b-values, and corresponding alterations in ADC values is another exciting area of future research. Hence, DWI-ADC maps can be proposed to be done along with conventional MRI sequences so that early and accurate diagnosis can be sought for better management.

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