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Correlation between Vertebral Marrow Fat Fraction in MRI Using DIXON Technique and BMD in DXA in Patients of Suspected Osteoporosis

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Abstract

Aim Osteoporosis is a common metabolic bone disease accounting for low back pain (LBP). It is diagnosed by dual-energy X-ray absorptiometry (DXA). Magnetic resonance imaging (MRI), a routine investigation for LBP, is also sensitive to detect fat fraction (FF) of the vertebral body that increases with increasing age. This study aimed to correlate vertebral marrow FF using MRI and bone mineral density (BMD).

Material and Methods Patients presenting with low backache and suspected osteoporosis were included. All patients underwent an MRI of lumbosacral spine and DXA. Patients were categorized into an osteoporotic and a nonosteoporotic group based on the T-score obtained from DXA. "T-scores" of < -2.5 on BMD were considered as osteoporotic spine. T-score of > -2.5 was considered as nonosteoporotic. The FF obtained from the DIXON sequence of MRI was correlated between the two groups.

Result Thirty-one patients were included with a mean age of 54.26 ± 11.6 years. Sixteen patients were osteoporotic based on the defined criteria in the methods. The mean vertebral marrow FF was significantly higher in the osteoporotic patients ($64.98 \pm 8.8\%$) compared with the nonosteoporotic ($45.18 \pm 13.2\%$) ($p = 0.001$). The mean FF of the vertebra having fracture ($69.19 \pm 7.73\%$) was significantly higher than that of patients without fracture ($57.96 \pm 5.75\%$) ($p = 0.03$). Taking a cutoff value of vertebral marrow FF of 54.85, the sensitivity and specificity of diagnosing osteoporosis were 93 and 80%, respectively, with a confidence interval of 95%. The area under the curve was 0.925.

Conclusion Increased vertebral marrow FF is noted in the osteoporotic spine. FF has an inverse correlation with the T-score obtained from BMD. MRI with FF measurement can provide indirect evidence of osteoporosis, which can be done under one roof, especially in young patients where we need to avoid ionizing radiation.

Keywords
- fat fraction
- vertebra
- osteoporosis
- IDEAL-IQ
- MRI
- back pain

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Introduction

Osteoporosis is a common metabolic disease characterized by reduction in bone strength. It predisposes the affected individual to an increased fracture risk that leads to poor quality of life. In the elderly age group, approximately 40% of females and 20% of males older than 50 years are affected by osteoporosis.[1,2] Early detection of osteopenia and osteoporosis and their management are crucial to prevent osteoporotic vertebral fracture.

Bone consists of mineralized and nonmineralized components. The cortex and trabeculae constitute the mineralized components whereas the bone marrow is the nonmineralized component. Bone mineral density (BMD) can be assessed using dual-energy X-ray absorptiometry (DXA) or quantitative computed tomography (CT) that quantitatively measures mineralized components.[3] Quantitative CT is not recommended as screening in suspected osteoporotic patients due to the risk of exposure to ionizing radiation.

Magnetic resonance imaging (MRI) is a noninvasive imaging modality for investigating the spine and its marrow. MRI can show gross morphological abnormality of the spine. It can also provide information based on chemical composition and at the cellular level. MRI does not use ionizing radiation, again adding to its advantage. Various studies have shown an inverse relation of BMD with vertebral fat content. The vertebral bone marrow FF can be assessed by using various MRI sequences such as T1-weighted imaging (T1WI), MR spectroscopy, and chemical shift imaging. T1WI is routinely acquired during an MRI of the lumbosacral spine. Few recent studies have introduced an M-score analog to the T-score of DXA based on the mean signal-to-noise ratio of the L1–L4 vertebral bodies in T1WI.[4–6] MR spectroscopy has been used for bone marrow fat quantification.[1,6] However, the technique is very time consuming and requires a trained operator to acquire the sequence. Unlike MR spectroscopy, which can detect the fat content in a small area of a single vertebra, DXA can find the mean BMD from the whole of the lumbar vertebral bodies.

Another new MRI method for fat quantification is the fat fraction (FF) estimation using the DIXON technique.[7] It is fast, does not require much technical skill, is easy to interpret, and all the lumbar vertebral levels can be included in a single acquisition. In this study, we aimed to evaluate the correlation between the FF of lumbar vertebra by using chemical shift imaging in MRI and the standard BMD.

Material and Methods

This cross-sectional observational study was performed after obtaining ethical approval from an institute ethics committee. Thirty-one patients with suspected osteoporosis who presented with low backache were included. Patients with a history of trauma and those having suspected or diagnosed vertebral neoplastic lesions were excluded from this study. All the patients underwent DXA examination of the lumbar vertebra (L1 to L4) using a Hologic Discovery dual-energy X-ray bone densitometer (Hologic Inc., Bedford, Massachusetts, United States). A "T-score" of < -2.5 on BMD was considered an osteoporotic spine. T-score of > -2.5 was considered as normal.[3,8]

The same patients also underwent MRI within 1 month (of the DXA scan). All the enrolled patients underwent an MRI of the lumbosacral spine in a 3T MRI scanner (GE, Discovery 750) using a 36-channel spine coil. MRI protocol was as follows: sagittal T1-weighted image with TR-690, TE-8.3, NEX-2, sagittal T2-weighted image withTR-4310, TE-88.8, coronal short tau inversion recovery (STIR); TR-11180, TE-71.3, TI 210. Axial T2WI was acquired at the level of intervertebral discs. All the scans were acquired with 4 mm thickness with a gap of 0.4 mm. Iterative decomposition of water and fat with echo asymmetry and least-squares estimation-intelligence quotient (IDEAL-IQ) was done in the sagittal plane, FOV 32×32 cm, NEX-2, TE-1.3 to 7.6, number of TEs per scan 9, and TR-10.5.

Image analysis was done in an Advantage Workstation Server (AWS) system provided by GE medical system. Morphological parameters of the lumbosacral spines, such as alignment, signal intensity of vertebra, degenerative change, anterior or central wedging, and compression fractures, were identified on sagittal T2WI and sagittal T1WI. Vertebral body height less than the height of the adjacent vertebra, central wedging, or anterior wedging was considered a fracture. The presence of vertebral marrow edema was identified on the STIR sequence. Vertebral body FF was obtained from the derived images from the acquired IDEAL-IQ sequence, which is a chemical shift imaging using six echo DIXON sequences.

Three region of interests (ROIs) were placed at the center of the vertebral body of L1, L2, L3, and L4 vertebrae in the midsagittal, right, and left parasagittal sections. The mean FF was calculated for individual vertebrae by averaging the values obtained from the three ROIs. The mean vertebral body FF was calculated by averaging the FF values of L1 to L4 vertebra (►**Fig. 1**). Three ROIs of size 100 to 180 mm^2 were kept at the center of the vertebral body of L1, L2, L3, and L4 vertebral bodies in the midsagittal and parasagittal sections. Care was taken to avoid intervertebral discs, the cortical bone of the vertebral bodies, focal vertebral lesions, the basivertebral venous plexus, fatty endplate changes, and the spinal canal. Fractured segment or marrow edema, if any, was also avoided, and ROI was placed in the remaining part of the vertebral body and the average value was taken (►**Fig. 2**). Thus, the ROI size was variable according to the available vertebral body area after excluding the abovementioned regions. We chose to take L1, L2, L3, and L4 vertebrae as BMD was available for these vertebrae. The mean vertebral marrow FF was obtained by averaging the FF of L1 to L4 vertebra. We also analyzed normalized vertebral FF obtained by dividing the mean vertebral FF by the FF of the subcutaneous fat.

Statistical analysis was done using SPSS version 20. Categorical data were presented as frequency and percentages. All measurements were described as mean value, standard deviations, and range. A nonparametric Mann–Whitney *U* test was done to compare FF between the osteoporotic and nonosteoporotic groups and among the osteoporotic

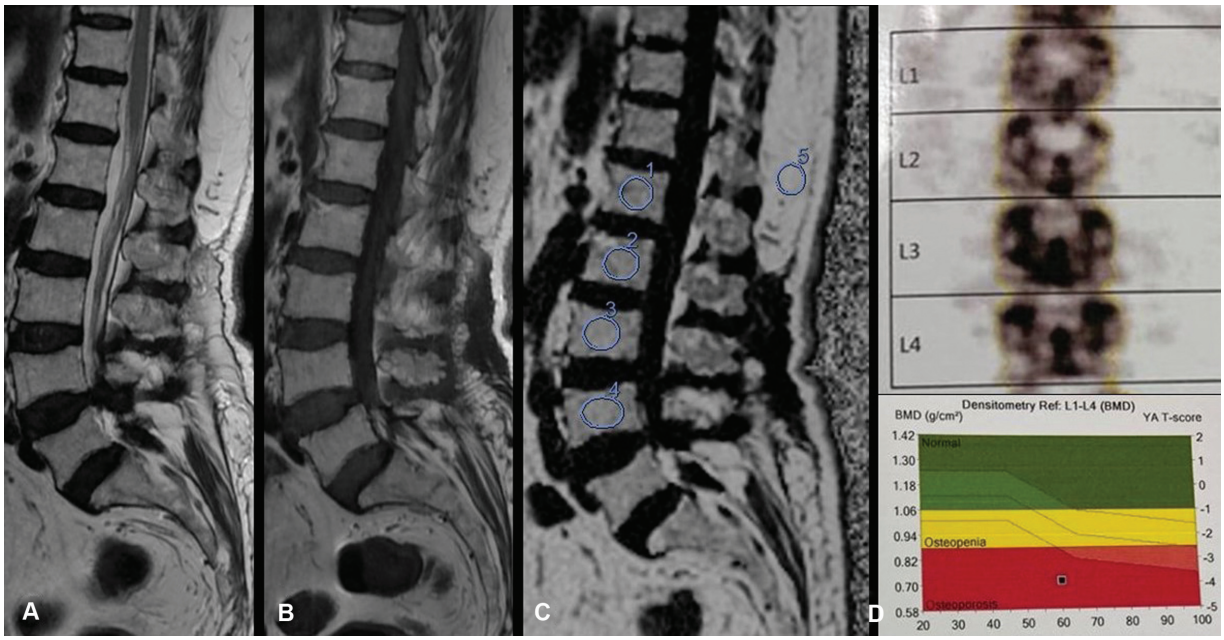

Fig. 1 Magnetic resonance imaging (MRI) lumbosacral spine and bone mineral density (BMD) in a 65-year-old female patient presenting with low backache. Routine T2-weighted imaging (T2WI) (**A**) and T1WI (**B**) show intervertebral disc desiccation at all levels and marginal osteophytes. Fat fraction (72) was obtained from iterative decomposition of water and fat with echo asymmetry and least-squares estimation-intelligence quotient (IDEAL-IQ) sequence. T-score of −3.9 was obtained from dual-energy X-ray absorptiometry (DXA) (**D**).

patients with and without a vertebral fracture. A p-value of < 0.05 was considered as significant. Spearman's correlation was done to find out any correlation between vertebral body FF of L1 to L4 vertebra with that of the T-score of L1 to L4 vertebra. Receiver operating curve (ROC) analysis was done to calculate the diagnostic accuracy of vertebral marrow FF, considering the T-score derived from DXA as a gold standard. Youden index was used to calculate the cutoff of vertebral marrow FF to differentiate the osteoporotic from the non-osteoporotic group.

Results

Thirty-one patients were included. Eight (25.8%) patients were male. The mean age of the included patients was 54.26 ± 11.6 years. Degenerative changes in the form of disc bulges, protrusion, extrusion, or osteophyte formation were found in all patients of the osteoporotic group and 73.3% in the nonosteoporotic group. Sixteen (51.6%) patients were osteoporotic according to the T-score on BMD and 15 (48.4%) were nonosteoporotic, considering a T-score of –2.5 as the cutoff value. Osteoporotic fracture was found in 10 out of 16 osteoporotic patients and none in the nonosteoporotic group.

The mean T-score of all participants was -2.64 ± 1.5 (–5.27 to 0.73). The mean vertebral marrow FF of all the participants was $54.94 \pm 14.8\%$. The mean vertebral marrow FF was significantly higher in the osteoporotic patients ($64.98 \pm 8.8\%$) compared with the nonosteoporotic ($45.18 \pm 13.2\%$) ($p = 0.001$). Details are given in ►**Table 1**. The mean normalized vertebral FF was significantly higher in osteoporotic patients (0.69 ± 0.09) than in nonosteoporotic (0.48 ± 0.13) ($p = 0.001$). On comparing FF from L1 to L4 vertebra between the osteoporosis and nonosteoporotic groups, there was a significant difference between the two groups at each level ($p = 0.001$) (►**Fig. 3**).

A subgroup analysis of the osteoporotic patients having vertebral fracture and without vertebral fracture was done. The mean duration of symptoms of patients having fracture was 18.1 ± 8.5 months, and for those without fracture was 9.7 ± 2.9 months, $p = 0.042$. The mean FF of the vertebra having fracture ($69.19 \pm 7.73\%$) was significantly higher than the mean FF of patients without fracture (57.96 ± 5.75) ($p = 0.03$). The mean T-score of the vertebra having fracture (-4.06 ± 0.75) was less than that of patients without fracture (-3.47 ± 0.77). However, the difference was not statistically significant ($p = 0.14$).

ROC showed a cutoff of vertebral marrow FF of 54.85, which can differentiate osteoporotic from nonosteoporotic vertebra with a sensitivity of 93% and specificity of 80%, with a 95% confidence interval (CI) and the area under the curve (AUC) of 0.925. With a cutoff value of a normalized FF of vertebra being 0.596, the osteoporotic vertebra can be differentiated from the nonosteoporotic vertebra with a sensitivity of 94% and specificity of 87%, with 95% CI and AUC of 0.929 (►**Fig. 4**). There was a strong inverse correlation between the FF of lumbar vertebra (L1 to L4) and the T-score ($p = 0.001$).

Discussion

Our study shows that the FF of vertebral marrow is higher in osteoporotic spine. FF also increases with increasing age. It could be due to various reasons. Fat content of the bone

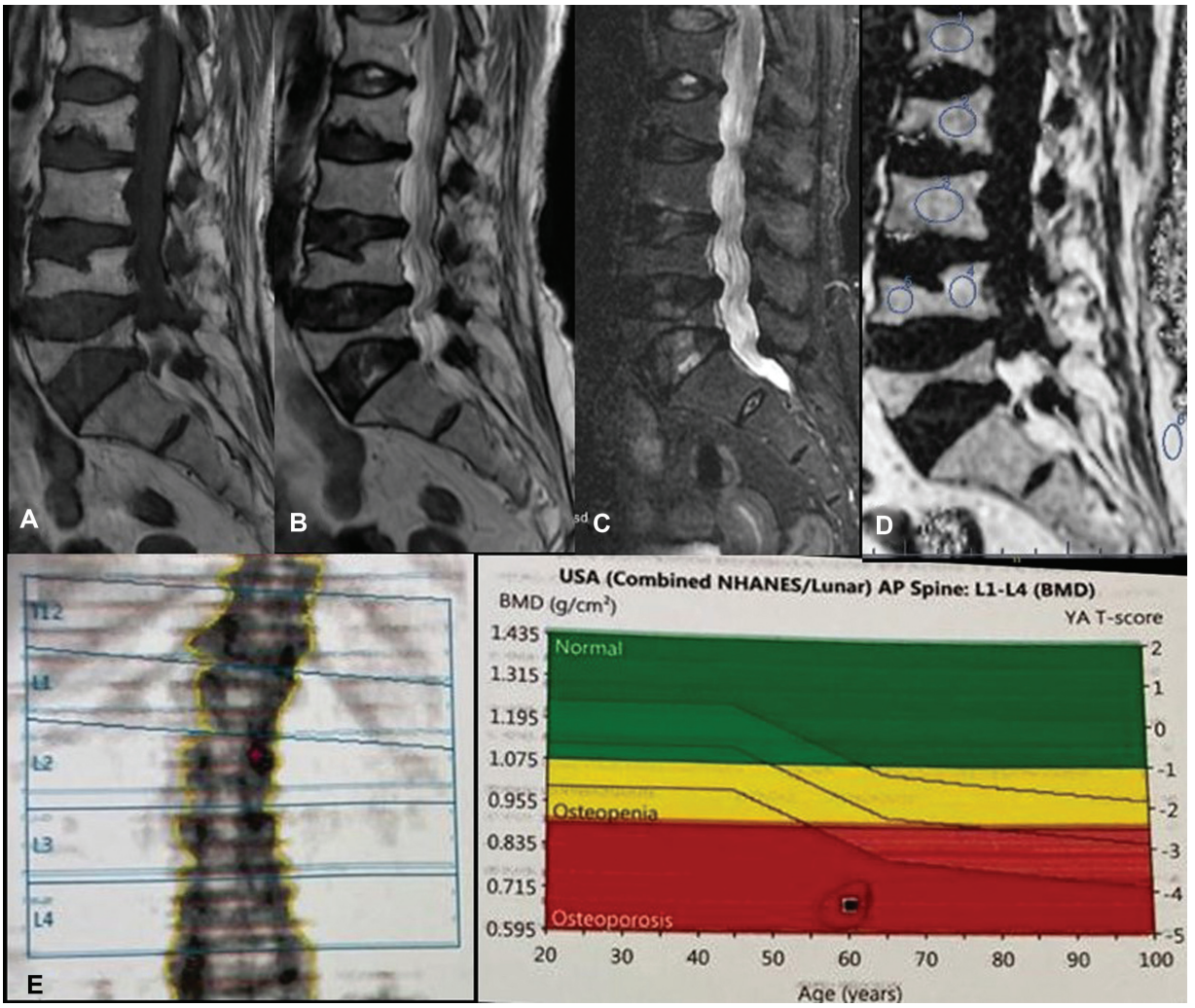

Fig. 2 Magnetic resonance imaging (MRI) lumbosacral spine and bone mineral density (BMD) in a 61-year-old osteoporotic female with vertebral fracture. Routine T1-weighted imaging (T1WI) (**A**) and T2WI (**B**) show intervertebral disc desiccation at all levels and marginal osteophytes, central wedging of L2, L4, and L5 vertebra. There was minimal focal marrow edema at the lower endplate of L3 vertebra on short tau inversion recovery (STIR) sequence (**C**). Fat fraction of 75 was obtained from iterative decomposition of water and fat with echo asymmetry and least-squares estimation-intelligence quotient (IDEAL-IQ) sequence (**D**). T-score of –4.2 was obtained from dual-energy X-ray absorptiometry (DXA) (**E**).

marrow increases with age and menopause. Atherosclerotic changes in intraosseous vessels also contribute to an increase in FF of the bone marrow.[1,6]

In early ages, the bone marrow is composed predominantly of red marrow. With aging, the red marrow gradually gets converted to yellow marrow containing a majority of adipocytes that vary depending on age, sex, and anatomical site. The bone marrow stem cells differentiate into bone, cartilage, and fat tissue under various endocrine and other complex regulatory factors. As the stem cell gives rise to both adipocytes as well as osteoblasts, increase in the fat content of the marrow can be associated with a low bone mass during osteoporosis, which is characterized by a decrease in BMD on DXA.[9]

In postmenopausal women, an increase in bone marrow fat content of the vertebral body is associated with decreased bone density and apparent diffusion coefficient.[10] Previous studies have shown that there is a correlation between bone marrow FF and BMD in both sexes. They could not get a significant difference in the vertebral FF between normal and osteopenic females.[1,6] Thus, the relationship between FF and bone density of the vertebra needs to be evaluated with a larger sample size, including both genders.

The change in the FF of vertebral bodies also varies in males and females. In males, FF increases sharply before the age of 25 years, and after that there is no significant increase. In contrast, there is a sharp increase in the FF after 45 years in female.[11] Studies have assessed bone marrow changes for diagnosing osteoporosis at an early stage. As increased FF is positively related to osteoporosis, assessment of vertebral marrow FF gives indirect evidence of osteoporosis.[11,12]

Recently, MRI has evolved as a noninvasive modality for the estimation of vertebral marrow FF. Another advantage is that it does not use any ionizing radiation. MR spectroscopy is the most widely accepted method for measuring FF in MRI. However, it has few limitations. First, the voxel can be kept in

Table 1: Demography, MRI findings, fat fraction (FF) of lumbar vertebra, and T-score of all patients and comparison between osteoporotic and non-osteoporotic group

Parameters	All patients included in the study (n = 31)	Osteoporosis group (n = 16)	Non-osteoporotic group (n = 15)	p-Value
Age in years, Mean ± SD (range)	54.26 ± 11.6 (33-74)	60.75 ± 7.31 (47-74)	47.33 ± 10.02 (33-67)	0.002
BMI (Kg/m2), Mean ± SD (range)	23.8 ± 3.87 (17.3-31.4)	23.33 ± 4.19 (17.3-31.2)	24.34 ± 3.56 (20.8-31.4)	0.304
Male:female	8:23	2:14	6:9	–
Vertebral body FF (%) at L1 (Mean ± SD)	52.98 ± 14.96	63.28 ± 9.63	41.99 ± 11.40	0.001
Vertebral body FF (%) at L2 (Mean ± SD)	54.60 ± 14.74	64.29 ± 9.46	44.26 ± 12.16	0.001
Vertebral body FF (%) at L3 (Mean ± SD)	55.67 ± 15.16	63.19 ± 9.38	45.52 ± 13.57	0.001
Vertebral body FF (%) at L4 (Mean ± SD)	56.53 ± 16.12	67.16 ± 10.38	45.19 ± 13.20	0.001
Mean vertebral body FF (%) (L1 to L4), Mean ± SD (range)	54.9 ± 14.8, (22.39-75.65)	64.98 ± 8.8, (46.46-75.65)	45.18 ± 13.2 (22.39-60.83)	0.001
Normalized FF, Mean ± SD (range)	0.59 ± 0.16 (0.23-0.81)	0.69 ± 0.09 (0.49-0.81)	0.48 ± 0.13 (0.23 to 0.65)	p = .001
Mean_T_score Mean ± SD (range)	-2.64 ± 1.51 (-5.27 to 0.73)	-3.83 ± 0.79 (-5.27 to -2.5)	-1.33 ± 0.91 (-2.23 to 0.73)	0.001
Presence of fracture	10	10 (62.5%)	None (0%)	–
Degenerative changes	27	16 (100%)	11 (73.33%)	–

Abbreviations: BMI, body mass index; MRI, magnetic resonance imaging; SD, standard deviation.

one vertebra at a time. Thus, it reflects fat content in a single vertebra. Second, MR spectroscopy is very time consuming and needs a trained operator.

A study by Kühn et al found that proton density FF was increased in osteoporotic compared with normal persons (*p*-value of 0.007).[12] However, they could not find a difference in FF between normal and vertebra with osteopenia. Another study has shown a negative correlation between average BMD and FF of vertebra. In their study, the FF was significantly higher in osteoporotic patients (62.53 ± 5.02) compared with a control group (51.25 ± 7.38), $p < 0.05$.[13] The vertebral FF has been found to be more in patients with vertebral fracture than without vertebral fracture.[14]

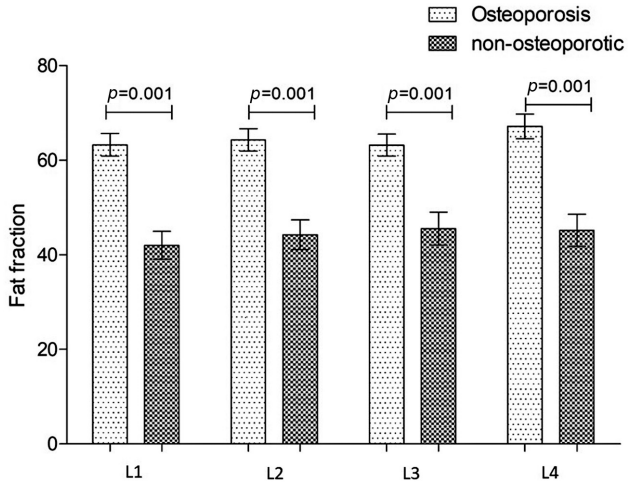

Fig. 3 Error bar diagram comparing fat fraction (FF) (%) from L1 to L4 vertebra between osteoporotic and nonosteoporotic group.

IDEAL sequence, which has become recently available, is based on the separation of fat and water. IDEAL-IQ is a highly reproducible chemical shift imaging that uses the six echo DIXON method to quantify FF by correcting confounding factors such as magnetic field inhomogeneity.[15,16] It allows measurements of fat in multiple vertebrae in a single scan and in a short time, and the results correspond closely with those of MR spectroscopy, which is considered to be a tested sequence for fat quantification in the vertebra. Studies have also shown the use of this method in characterizing vertebral lesions.[17] We have evaluated the FF of the vertebra using this technique. Our study showed an increased FF in cases of osteoporosis compared with the nonosteoporotic group. We also found an increased FF in patients with osteoporotic fractures than those without fractures.

Fracture is the most important clinical outcome of osteoporosis, which sometimes goes unnoticed and incidentally detected on radiological imaging. There is a five times increased risk of a repeat vertebral fracture in osteoporosis patients having vertebral fracture.[18] In this study, we found that the mean FF of osteoporotic spine having vertebral fracture was significantly higher than those without fracture ($p = 0.03$).

There are a few limitations in our study. The number of included patients was less. We could not compare between osteoporotic, osteopenia, and normal groups. Most of the enrolled patients in the osteoporotic group of our study were females, lacking information about males. Therefore, the gender representativeness of the sample was insufficient.

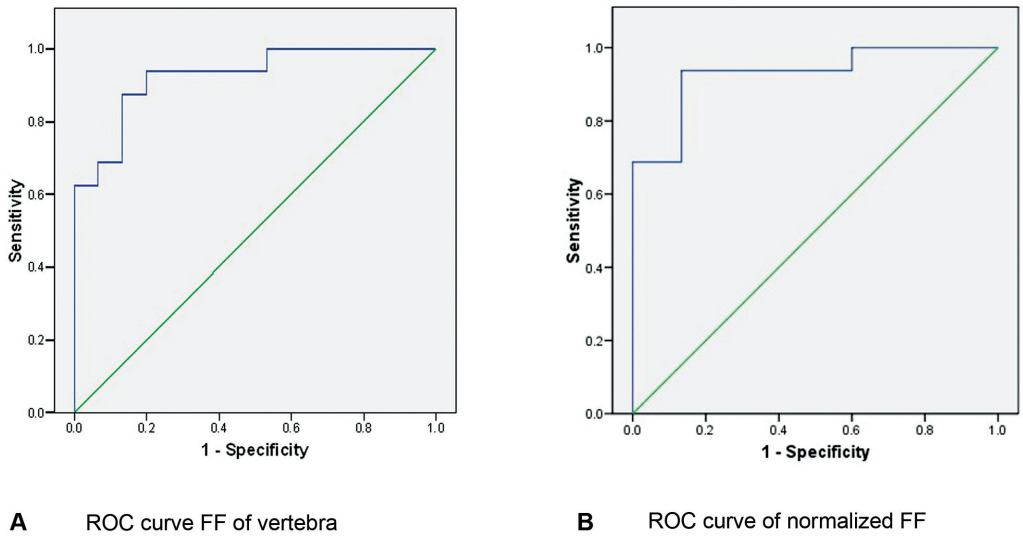

Fig. 4 Receiver operating curve (ROC) for (**A**) fat fraction of vertebra and (**B**) normalized fat fraction of vertebra. FF, fat fraction.

Further investigation with a large sample size is required for generalization.

Conclusion

MRI gives new insight into the bone composition of the vertebra. Increased vertebral marrow FF is noted in the osteoporotic spine. FF has an inverse correlation with the T-score obtained from BMD. Calculation of vertebral marrow FF using MRI is a noninvasive technique that does not use ionizing radiation and can be an alternative technique for osteoporotic patients.

Informed Consent

Informed consent was obtained from all the patients included in the study.

Authors' Contributions

S.N. contributed with conceptualisation, design, data analysis, literature search, manuscript editing, and manuscript review. M.J. contributed with conceptualisation, design, data analysis, literature search, manuscript editing, and manuscript review. S.K.B. took part in data analysis, literature search, manuscript editing, and manuscript review. S.T. contributed with literature search, manuscript editing, and manuscript review.

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Conflict of Interest

None declared.

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