

## Lumbar Spine MRI Signal Intensity Measurements in The Assessment of Abnormal Bone Mineral Density in Postmenopausal Women

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### Abstract

<b>Background</b>	Osteoporosis is characterized by low bone mass and micro-architectural deterioration.
<b>Objective</b>	To measure a quantitative magnetic resonance imaging (MRI)-based score (M-score) for the diagnosis of abnormal bone mineral density in postmenopausal female and compare the results with standard control taking dual-energy x-ray absorptiometry (DEXA) scan measurements as a reference.
<b>Methods</b>	This case-control study was conducted with 50 postmenopausal females who underwent DEXA exam for back pain. Another 50 healthy young females aged 20-29 years were used as a control group, and an MRI of the lumbar spine was done to all participants. From sagittal T1-weighted spin-echo sequence, Signal to noise ratio of L1-L4 was measured to all patients and controls and used to obtain M-score.
<b>Results</b>	DEXA revealed that 19 patients had a normal T-score, 14 patients had osteopenia, and 17 patients had osteoporosis (mean T score -1.737), M-score were significantly higher among cases than controls ( $P = 0.0001$ ). The SNR L1-L4 and M-score are negatively correlated to T-score ( $r = -0.864$ ; $P = 0.0001$ ) and bone mineral density (BMD) ( $r = -0.863$ ; $P = 0.0001$ ). The receiver operator characteristic (ROC) analysis revealed an M-score threshold of 2.63434 with 88.2% sensitivity and 78.8% specificity ( $P = 0.0001$ ) for the discrimination of osteoporotic from non-osteoporotic females. For distinguishing normal from low-BMD patients, the ROC curve estimated an M-score threshold of 1.34413 with 100% sensitivity and specificity ( $P = 0.0001$ ). According to the calculated M-score, 19 patients were normal (M-score $<1.334$ ), 9 patients found to have osteopenia (M-score 1.334 - 2.634), and 22 osteoporotic patients (M-score $>2.634$ ).
<b>Conclusion</b>	M-score obtained from T1WI sequence of lumbar spine study is a useful quantitative method for the diagnosis of osteoporosis and osteopenia in postmenopausal females as compared to DEXA scan. The best cut off value for osteoporosis is 2.634. The best cut off value for osteopenia is 1.344.
<b>Keywords</b>	Lumbar spine MRI, postmenopausal women, bone mineral density
<b>Citation</b>	Mudhahir DA, Kadhim MA. Lumbar spine MRI signal intensity measurements in the assessment of abnormal bone mineral density in postmenopausal women. Iraqi JMS. 2025; 23(2): 255-263. doi: <a href="https://doi.org/10.22578/IJMS.23.2.8">10.22578/IJMS.23.2.8</a>

**List of abbreviations:** BMD = Bone mineral density, DEXA = Dual energy x-ray absorptiometry, ROC = Receiver operator characteristic, SNR = Signal-to-noise ratio

### Introduction

Osteoporosis is a disease characterized by low bone mass, deterioration of bone tissue, and disruption of bone microarchitecture: it can lead to an increase in

the risk of fractures. World Health Organization (WHO) has estimated that 30% of all women aged over 50 (postmenopausal) have osteoporosis <sup>(1)</sup>. Dual-energy x-ray absorptiometry (DEXA) is considered the gold standard for the diagnosis of osteoporosis <sup>(2)</sup>. However, there are considerable errors in DEXA measurements arising from the inhomogeneous distribution of adipose tissue <sup>(3)</sup>. The definition of osteoporosis is based on the T-score, which is the difference between the measured bone mineral density (BMD) and the mean value of young adults, expressed in standard deviations (SD) for a normal population of the same gender and ethnicity. DEXA reports also provide Z-scores, which are calculated similarly to the T-score, except that the patient's BMD is compared with an age-matched mean <sup>(4)</sup>. Normal BMD is defined as a T-score between (+2.5 and -1), osteopenia (low BMD) is defined as a T-score between (-1.0 and -2.5), osteoporosis is defined as a T-score below (-2.5) and severe osteoporosis is defined as a T-score below (-2.5) in the presence of one or more fragility fractures <sup>(5)</sup>.

Lumbar spine magnetic resonance imaging (MRI) is an imaging examination frequently requested worldwide mainly due to low back pain <sup>(6)</sup>. The routine spine evaluation typically includes T1 and T2 weighted sequences in axial and sagittal planes <sup>(7)</sup>. T1-weighted spin-echo (SE) images are best to evaluate the cellular content in bone marrow <sup>(8)</sup>.

MRI has demonstrated considerable potential in the quantitative assessment of cancellous bone architecture *in vivo* <sup>(9)</sup>. It was demonstrated that a decrease in cancellous bone was accompanied by a corresponding increase in fat cells in the bone marrow. Osteoporosis has been shown to be associated with increased fat content in the marrow <sup>(10)</sup>. It was suggested by certain studies that bone marrow adipose tissue (BMAT) might play a role in the pathogenesis of osteoporosis <sup>(11,12)</sup>. MRI-measured pelvic, hip, and lumbar spine BMAT is negatively correlated with DEXA-measured hip and lumbar spine BMD <sup>(13)</sup>.

The purpose of the study is to measure a quantitative MRI-based score for the diagnosis of abnormal BMD in postmenopausal women and to compare the results with standard control taking DEXA scan measurements as a reference.

## **Methods**

### **Study group**

Single-center case-control study was conducted between July 2021 and December 2021 in Al-Imamein Al-Kadhimein Medical City, Baghdad, Iraq. The study was approved by the Scientific Committee of the Iraqi Board of Diagnostic Radiology.

One hundred participants were included in the study, 50 patients were postmenopausal females chosen from the patients that had undergone DEXA scan for lower back pain, and 50 females were taken as a control. A lumbar MRI scan was done to all the patients and controls.

### **Inclusion criteria**

Female postmenopausal patients with suspected abnormality in BMD.

### **Exclusion criteria**

Oncology patients, traumatic vertebral injuries, general contraindications to MRI, and patients refusing to participate in the study.

To calculate an MRI-based score equivalent to the T-score used in DEXA, a reference group of 50 healthy females aged 20 - 29 years who had undergone a lumbar MRI for low back pain was used. The same exclusion criteria were applied in addition to excluding any study with intra venous contrast injection.

### **MRI**

All examinations were performed at 1.5T MR System (Magnetom Avanto, Siemens Healthineers, Germany). The routine imaging protocol was performed, including sagittal T1Weighted Image (WI)m sagittal T2WI, axial T2WI, and MR myelography. All the

measurements in this study were taken from the sagittal T1-weighted spin-echo sequence, optimal for evaluating vertebral fatty marrow (TR = 550 ms, TE = 9.9 ms, slice thickness = 4 mm; squared field of view = 333 mm).

The vertebral bodies from L1-L4 were evaluated. A region of interest (ROI) was manually placed as a circle in the vertebral body, excluding cortical bone, subchondral abnormalities, focal lesions (e.g., hemangiomas), and posterior venous plexus, 3 ROIs were acquired for each vertebral body on different sagittal slices, with their mean used for analysis. Another ROI with the same size was taken in an artifact-free site outside the patient to measure the noise. Signal-to-noise ratio (SNR) was calculated for each vertebra and obtained by dividing the intra-vertebral signal intensity by the standard deviation of the noise. Then for each patient, the median value of vertebral bodies SNRs from L1 to L4 was calculated (SNR L1-L4). The diagnostic performance of SNR L1-L4 was estimated for each patient and used to obtain an M-score based on the calculation formula of T-score for the diagnosis of osteoporosis. The SNR L1-L4 of the control group was also used in the equation by using their mean (SNR ref) and SD ref. The M-score was defined according to the formula<sup>(14)</sup> as follows:

$$\text{M-score} = (\text{SNR (L1-L4)} - \text{SNR ref}) / (\text{SD ref})$$

#### DEXA scan

For the lumbar spine was done by using STRATOS device (DMS group imaging, France) in the supine position. BMDs of lumbar vertebrae (L1-L4) were automatically obtained, and BMD values were calculated using T-score.

#### Statistical analysis

It was carried out using statistical package of SPSS-27 (Statistical Packages for Social Sciences- version 27). The significance of BMD and T score differences on DEXA, SNR (L1-L4), and M-score on MRI were tested using Students-t-test for the difference between two independent means or ANOVA test for

difference among more than two independent means. Chi-squared test was used for analyzing differences between the results of MRI (calculated M-score) and DEXA scan. Sensitivity and specificity of MRI were calculated and compared. Statistical significance was considered whenever P value was  $\leq 0.05$ . Receiver operating curve (ROC) analysis was used to estimate the diagnostic performance of SNR L1-L4 using lumbar vertebral DEXA as a reference and to define the cutoff values of M-score and SNR L1-L4 for the discrimination of osteoporotic from non-osteoporotic females.

#### Results

The study include includes 50 postmenopausal women with a mean age of  $61.1 \pm 5.8$  years (age range 53 - 73 years) and 50 young, healthy females, their mean age  $25.6 \pm 2.6$  years (age range 21 - 29 years). Regarding DEXA measurements 19 patients (38%) had a normal T-score ( $>1.0$ ), 14 patients (28%) had osteopenia (-1.0 - -2.49), and 17 patients (34%) had osteoporosis ( $\geq -2.5$ ) with a mean T score of  $-1.737 \pm 1.338$  (range -4.100 - 0.630), the BMD values show a mean of  $0.854 \pm 0.147$  (range 0.593 - 1.116).

#### MRI results

SNR L1-L4 and M-score were significantly higher among cases than control. For the postmenopausal patients, the mean SNR L1-L4 was  $353.55 \pm 201.04$  (range 55.79 - 728.24) while in the control group was  $104.81 \pm 55.21$  (range 31.23 - 219.68), which is highly significant ( $P = 0.0001$ ), and after the calculation of the M-score, the postmenopausal patients showed significantly higher values (their mean  $2.075 \pm 1.782$ ) and a range (-0.564-5.397) compared to the control group which had a mean M-score of  $-0.128 \pm 0.488$  a range of (-0.742 - 0.889).

#### Correlation between DEXA and MRI findings

There was a highly significant correlation between the DEXA parameters and the MRI results. The study showed that SNR L1-L4 was

negatively correlated to T-score ( $r = -0.864$ ;  $P = 0.0001$ ) and BMD ( $r = -0.863$ ;  $P = 0.0001$ ). The study revealed that M-score was also

negatively correlated with T-score ( $r = -0.864$ ;  $P = 0.0001$ ) and BMD ( $r = -0.863$ ;  $P = 0.0001$ ) (Table 1).

**Table 1. Correlation between DEXA and MRI parameters**

<b>Postmenopausal</b>		<b>DEXA BMD</b>	<b>DEXA T-score</b>	<b>SNR L1-L4</b>	<b>MRI M-score</b>
Age (years)	r	-0.481**	-0.484**	0.426**	0.426**
	P	0.0001	0.0001	0.002	0.002
DEXA BMD	r	-	-	-0.863**	-0.863**
	P	-	-	0.0001	0.0001
DEXA T-score	r	-	-	-0.864**	-0.864**
	P	-	-	0.0001	0.0001

\* Correlation is significant at the 0.05 level. \*\* Correlation is highly significant at the 0.01 level

When the values of the SNR L1-L4 and M-scores were distributed according to the T score standards, there was a clear cutoff for distinguishing normal from abnormal BMD on MRI, but the differentiation between osteopenia and osteoporosis showed an area of overlapping results.

The ROC curve assessment of M-score and SNR L1-L4 for discrimination of osteoporotic from non-osteoporotic females revealed  $AUC = 0.907$  at 95% confidence interval (0.829-0.986) and the diagnostic capability of using an SNR

L1-L4 threshold of 416.59359 and M-score threshold of 2.63434 with 88.2% sensitivity and 78.8% specificity,  $P = 0.0001$  (Figure 1A, Table 2).

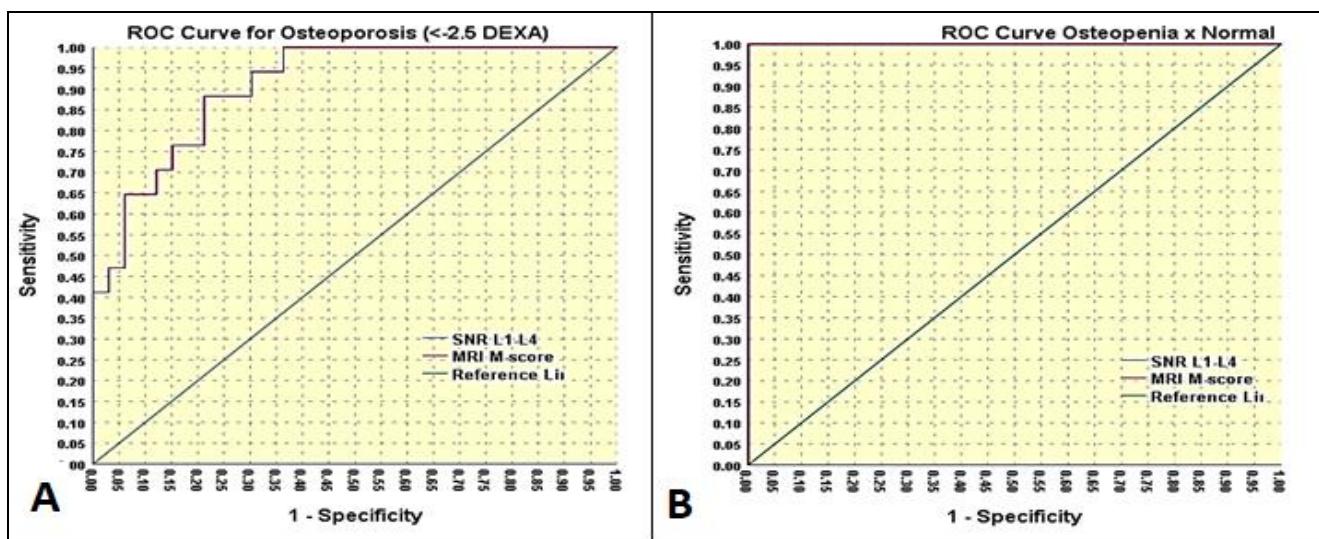
Meanwhile, the ROC curve assessment of SNR L1-L4 and M-score for the discrimination of normal from low-BMD patients revealed that  $AUC = 1.000$  at 95% confidence interval and the diagnostic capability of using an SNR L1-L4 threshold of 271.05644 and M-score threshold of 1.34413 with 100% sensitivity and specificity,  $P = 0.0001$  (Figure 1B, Table 3).

**Table 2. Parameters of the ROC curve with sensitivity and specificity of different values to differentiate osteoporotic from non-osteoporotic individuals**

<b>Variables</b>	<b>Area Under the Curve (AUC.)</b>	<b>Std. Error</b>	<b>P value</b>	<b>95% Confidence Interval</b>	
				<b>Lower Bound</b>	<b>Upper Bound</b>
SNR L1-L4	0.907	0.040	0.0001	0.829	0.986
MRI M-score	0.907	0.040	0.0001	0.829	0.986
<b>Coordinates of the Curve</b>					
<b>Variables</b>	<b>Positive if greater than or equal to</b>		<b>Sensitivity</b>	<b>Specificity</b>	
<b>SNR L1-L4</b>	373.66006			94.1	69.7
	<b>416.59359</b>			<b>88.2</b>	<b>78.8</b>
	433.68320			76.5	78.8
<b>MRI M-score</b>	2.25372			94.1	69.7
	<b>2.63434</b>			<b>88.2</b>	<b>78.8</b>
	2.78584			76.5	78.8

**Table 3.** Parameters of the ROC curve with sensitivity and specificity of different values to differentiate normal from low BMD values

Variables	Area Under the Curve (AUC.)	Std. Error	P value	95% Confidence Interval	
SNR L1-L4	1.000	0.0001	0.0001	-	-
MRI M-score	1.000	0.0001	0.0001	-	-
Variables	Coordinates of the Curve			Lower Bound	Upper Bound
Variables	Positive if greater than or equal to			Sensitivity	Specificity
SNR L1-L4	271.05644			100	100
MRI M-score	1.34413			100	100

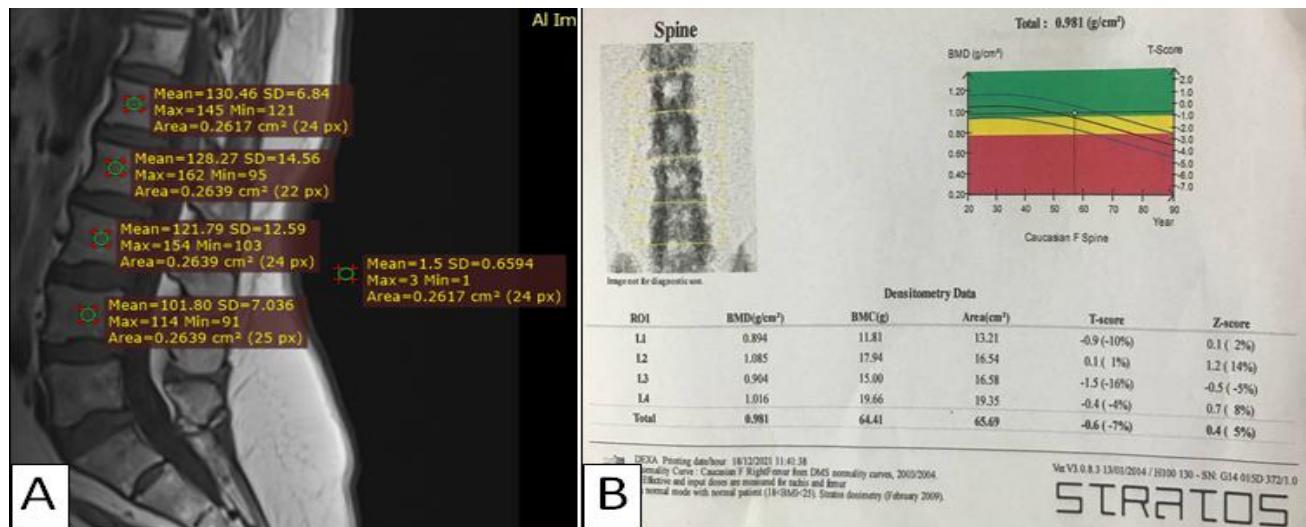
**Figure 1.** A: The ROC curve analysis of SNR L1-L4 and M-score to differentiate osteoporotic from non-osteoporotic individuals. B: The ROC curve analysis of SNR L1-L4 and M-score to differentiate normal from low BMD values

According to the calculated M-score by the ROC analysis, 19 patients were normal with an M-score less than 1.334, 9 patients were found to have osteopenia (M-score 1.334 - 2.634), and 22 osteoporotic patients (M-score >2.634).

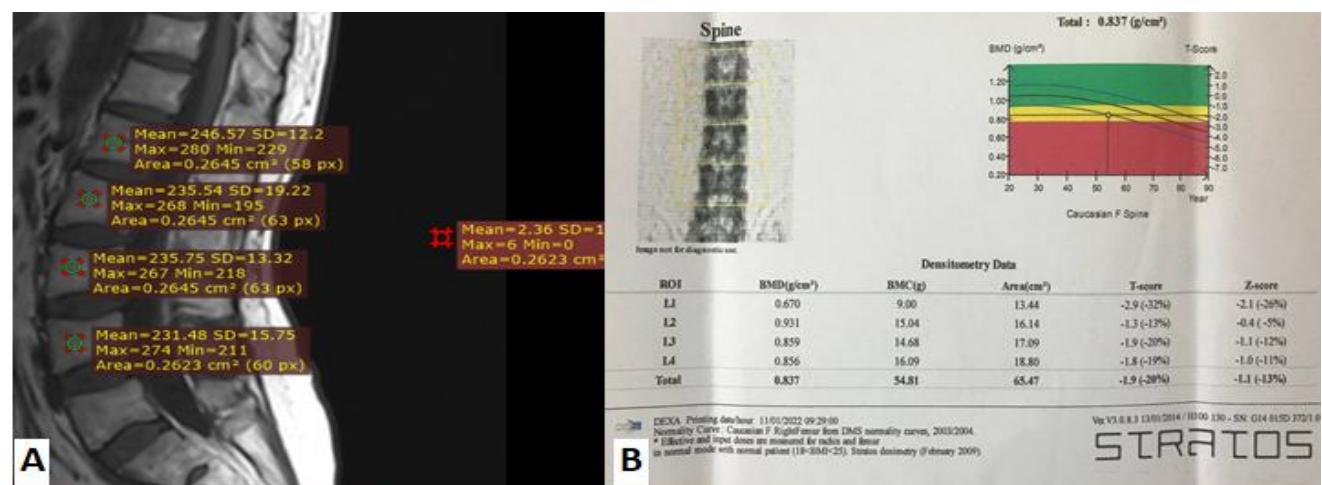
A comparison between the results of the DEXA and MRI findings was made as shown in table (4). Figures 2 and 3 show images of selected cases from this study.

**Table 4.** Comparison between the results of the DEXA and MRI

Results	DEXA		MRI	
	T score	No. of patients	M-score	No. of patients
Normal	>-1.0	19	<1.334	19
Osteopenia	-1.0--2.5	14	1.334-2.634	9
Osteoporosis	≥-2.5	17	>2.634	22



**Figure 2. Fifty-five-year-old woman with a BMI of 34 kg/m<sup>2</sup>. A: shows a sagittal T1-weighted magnetic resonance image of the lumbar spine. SI is measured on four ROIs manually segmented (L1, L2, L3, and L4), plus an ROI placed outside the patient to measure the noise. B: shows the DEXA report. T-score = -0.6 and M-score = 1.07, both in the normal range**



**Figure 3. Fifty-seven-year-old woman with a BMI of 19.23 kg/m<sup>2</sup>. A: shows a sagittal T1WI of the lumbar spine. SI is measured on four ROIs manually segmented (L1, L2, L3, and L4), plus an ROI placed outside the patient to measure the noise. B shows the DEXA report. T-score = -1.9 is in the osteopenia range, while M-score = 3.66 is in the range of osteoporosis**

## Discussion

As prevalence and awareness of osteoporosis increase and treatments of proven efficacy become available, the demand for management of patients with the disease will also rise. Such demand will, require widespread development of facilities for the diagnosis and assessment of osteoporosis<sup>(15)</sup>. Although DEXA

represents the gold standard quantitative imaging technique in the diagnosis of osteoporosis<sup>(16)</sup>, there are some limitations in its application, mainly due to osteoarthritis of the spine being present in a large proportion of the postmenopausal patients, soft tissue calcification (especially aortic calcification) and extreme obesity<sup>(17)</sup>. MRI of the lumbar spine is

a widely performed examination for low back pain <sup>(18)</sup> and considered the best imaging technique for investigating the causes of back pain. MRI is an ideal imaging technique for non-invasively investigating the properties of bone marrow fat <sup>(19)</sup>.

Despite the small sample of the current study, which doesn't permit to measure a prevalence for osteoporosis, it's concerning to notice that more than half of the cases (66%) were having abnormal BMD status, other studies in the Middle East region that share a lot of the environmental and lifestyle factors with our community, have shown a high prevalence of osteoporosis among postmenopausal women; the prevalence in Lebanon is estimated to be 31% according to WHO criteria <sup>(20)</sup>, in Kuwait, the prevalence was about 15% <sup>(21)</sup>, and in Saudi Arabia, the prevalence of osteoporosis among postmenopausal women was estimated in the range 35 - 48% <sup>(22)</sup>.

In the current study, SNR L1-L4 was higher in postmenopausal women than the normal control ( $353.545 \pm 201.038$  versus  $104.808 \pm 55.214$ ), the results of the current study was slightly higher than that shown by Shayganfar et al. <sup>(23)</sup> study (256.88). On the other hand, Bandirali et al. <sup>(14)</sup> showed a much lower mean value for the SNR L1-L4 (38) with a range of (29-58). These different results may be attributed to using different calibrated instruments as it is a device-dependent measurement, just like the BMD on DEXA devices. That necessitates a score to avoid the calibration differences, so a quantitative score was introduced (M-score) on the model of T score by Bandirali et al. <sup>(14)</sup>.

The current study found a mean of  $2.075 \pm 1.782$  for the M-score among the cases and  $-0.128 \pm 0.488$  among the controls with high statistical significance; this was in agreement with Shayganfar et al. <sup>(23)</sup> with a Mean of M-scores 1.76 (range -0.9 - 4.94).

The MRI and DEXA parameters in the present study have shown a highly significant negative correlation, i.e., the lower the BMD and T scores on DEXA, the higher their corresponding SNR L1-L4 and M-scores on MRI; this was in accordance with Saad et al. <sup>(24)</sup> revealing M-score was negatively correlated with T score

and BMD ( $P$  value  $<0.0001$ ). Bandirali et al. <sup>(14)</sup> concluded that SNR in L1-L4 are negatively related to BMD; also, the study has calculated a threshold for M-score to help in the diagnosis of osteoporosis in the patients being investigated with routine lumbar MRI.

In this study, it was found that the threshold of M-score for the diagnosis of osteoporosis was 2.634 with a sensitivity of 88.2%, specificity 78.8% with AUC was 0.907, and this means that for every 100 patients with M-score  $\geq 2.634$ , 88 patients will be truly identified as to have osteoporosis. This also means that for every 100 patients with M-score  $<2.634$ , 79 subjects will be correctly identified as not having osteoporosis. In Bandirali et al. <sup>(14)</sup> study, the demonstrated threshold of M-score was 2.5 with a sensitivity of 88% and specificity of 64%. Another proximate M-score threshold calculated by Shayganfar et al. <sup>(23)</sup> was 2.05 for distinguishing osteoporotic patients from non-osteoporotic individuals with a sensitivity of near 90%, specificity of near 87%. A higher threshold was found in Saad et al. <sup>(24)</sup> study with an M-score of 3.5 for diagnosing osteoporosis with a sensitivity of 93.3% and specificity of 83.5%.

For distinguishing normal from low bone mineral density, another threshold was calculated in the current study; an M-score of 1.344 was found to represent the cutoff between normal individuals and those with osteopenia with 100% sensitivity and specificity. This cutoff was found to be 2.2 by Saad et al. <sup>(24)</sup>, with a sensitivity of 92% and specificity of 98%. The differences in the threshold of M-score could be due to the differences in the sample size, type of population affected by the environmental and lifestyle factors, in addition to the differences between the MR systems used.

In the current study and according to the calculated M-score, 19 patients were normal (same number detected by DEXA), 9 patients were found to have osteopenia (compared to 14 patients diagnosed by DEXA), and 22 osteoporotic patients (in comparison to 17 diagnosed by DEXA). The elevated percentage of osteoporosis on MRI results was also noticed by Shayganfar et al. <sup>(23)</sup>, with 37.8% of

postmenopausal females were osteoporotic using M-score as compared to 35%, applying T-score, with a similar drop in the number of osteopenia cases from 19.4% by T score to 15.9% when using M-score. An explanation for this finding could be due to the degenerative changes with the advanced age in postmenopausal females that can give a false impression of higher T-scores. At the same time, MRI is not affected by spinal degenerative joint disease and can be more sensitive in the detection of osteoporosis. In Bandirali et al. (14) study, patients with degenerative changes were separated in the analysis of their results, which showed the highest degree of discordance between the DEXA and MRI results, with most of them, were underestimated by the DEXA.

In conclusion, the M-score obtained from the routine T1WI sequence of lumbar spine study is a useful quantitative method for the diagnosis of osteoporosis and osteopenia in postmenopausal women as compared to the gold standard DEXA scan examination. The best cut off value for osteoporosis is 2.634. The best cut off value for osteopenia is 1.344.

### **Acknowledgement**

Special thanks to Afrah Akram and Hayat Abed from the DEXA department for their valuable assistance.

### **Author contribution**

Dr. Mudhahir: designed the study and performed the study examinations on the patients. Dr. Kadhim: assisted in the measurements and analysis of the data, both authors discussed the results.

### **Conflict of interest**

There is no conflict of interest.

### **Funding**

self-funding.

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Received Oct. 25<sup>th</sup> 2023

Accepted Aug. 28<sup>th</sup> 2024