Received:
05 September 2018

Revised:
24 January 2019

Accepted:
01 February 2019

<https://doi.org/10.1259/bjr.20180774>

Cite this article as:

Shayganfar A, Khodayi M, Ebrahimian S, Tabrizi Z. Quantitative diagnosis of osteoporosis using lumbar spine signal intensity in magnetic resonance imaging. *Br J Radiol* 2019; **92**: 20180774.

FULL PAPER

Quantitative diagnosis of osteoporosis using lumbar spine signal intensity in magnetic resonance imaging

AZIN SHAYGANFAR, MAEDE KHODAYI, SHADI EBRAHIMIAN and ZHALE TABRIZI

Department of Radiology, Isfahan University of Medical Sciences, Isfahan, Iran

Address correspondence to: Dr Shadi Ebrahimian
E-mail: shadiebr2005@yahoo.com

Objective: Osteoporosis is the most common metabolic bone disease that is not recognized in many elderly people. To determine the cause of low back pain, lumbosacral MRI is done for a large population who may not have gone under dual energy X-ray absorptiometry (DXA). The aim of this study was to predict bone density using lumbar spine signals in lumbosacral MRI in high risk patients for osteoporosis including post-menopausal females and calculate a threshold for a new quantitative MRI-based score to be used in estimation of lumbar spine bone mass density.

Methods: 82 menopausal females, who had undergone DXA before, were selected and MRI was done within 6 months after DXA. 69 healthy females aged 20–29 years who had undergone lumbar MRI were selected as

reference group. Results were analyzed and threshold and diagnostic performance of MRI-based score (M-score) on the method of T-score was calculated.

Results: Negative correlation between M-score and T-score was detected. Cut off point of 2.05 was found for M-score with near sensitivity of 90% and specificity of 87% for detecting osteoporotic patients from non-osteoporotic individuals.

Conclusion: M-score is a MRI-based method which can identify patients at risk of osteoporosis. Early diagnosis of osteoporosis can reduce morbidity and mortality caused by it.

Advances in knowledge: The research introduced cut of points for M-score as a new MRI quantitative method to be used as an opportunistic technique for detecting osteoporotic patients.

INTRODUCTION

Osteoporosis is the reduction of bone mass and disruption of bone microarchitecture involving 55% of the population aged over 50 years.^{1,2} Risk of osteoporotic fractures increases with reduction of bone mass density (BMD).³ Osteoporosis is diagnosed using dual-energy X-ray absorptiometry (DXA) measuring bone mass density and is defined as T-score ≤ -2.5 at hip, spine or femur.⁴

Because osteoporosis is an asymptomatic disease, there are so many patients who do not undergo DXA despite the necessity of BMD testing and remained undiagnosed,⁵ while they may undergo MRI because of low back pain and complications caused by osteoporosis. A strong inverse correlation was observed between MRI measured pelvic and total bone marrow adipose tissue and BMD measured by DXA.⁶ It seems that in osteoporotic patients, fat content in vertebral marrow increases as bone density decreases.⁷ Studies have shown that bone marrow fat tissue is significantly higher in osteoporotic patients and there is an inverse relationship between BMD and adipose tissue in vertebral bone marrow.^{8,9} Higher rates of fragility fracture

were also reported in those with higher rate of fat content.¹⁰ Standard T_1 weighted images are validated by quantitative method for adipose tissue volume measurement and are the best for detection of cellularity and adipose tissue in bone marrow.^{11,12} An inverse relationship between bone marrow adipose tissue and BMD was observed in T_1 weighted images of lumbar spine of healthy middle aged males and females.¹³

Despite the correlation between adipose tissue seen in T_1 weighted images and BMD measured by DXA, MRI cannot be used as a tool for screening patients with osteoporosis due to lack of a quantitative score. Bandirali et al presented a new quantitative lumbar spine MRI based method on T_1 weighted images, suggesting signal-to-noise ratio (SNR) in L1–L4 and M-score in detection of osteoporosis.¹⁴ M-score is a score obtained from MRI on the model of T-score, using SNR instead of BMD. Based on mentioned study, SNR in L1–L4 vertebrae is negatively related to BMD, also M-score ≥ 5.5 in MRI is related to T-score ≤ -2.5 in DXA.¹⁴ These thresholds allow physicians to use MRI which is done to determine causes of low back pain, as an opportunistic

method to find individuals with osteoporosis who may need therapeutic interventions.

Due to the lack of a similar study in Iranian population, this study was performed to find sensitivity, specificity and diagnostic performance of M-score, having lumbar spine BMD measured by DXA as reference group, in Iranian society.

METHODS AND MATERIALS

Study group

This was a prospective study that began in June 2016 in Askariye BMD center, Isfahan, Iran and AL Zahra hospital, Isfahan, Iran. The study was approved by the internal review board of Isfahan radiology department.

82 menopausal females were chosen randomly from all post-menopausal females that had undergone DXA in BMD center of Askariye hospital from June 2017 to September 2017.

Individuals with the history of cancer, traumatic injury to the spine, demyelinating nerve disease, metal prosthesis, claustrophobia and those with more than one-unit difference between vertebral T-scores were excluded from the study.¹⁵

69 females aged 20–29 years who had undergone a lumbar MRI in Alzahra hospital because of low back pain were chosen randomly for use as the reference group for calculation of MRI-based M-Score.¹⁵ Those with history of systemic disease (hyperthyroidism, diabetes mellitus etc.) and use of drugs related to loss of BMD (anti-epileptic drugs, corticosteroids, chemotherapeutic medications etc.) were excluded from the study.

The purpose of the study was explained to all the patients and a written informed consent form was signed by them.

MRI

Post-menopausal females underwent MRI within 6 months after DXA examination. All the images were performed by a 1.5 T MRI (Philips Ingenia, Eindhoven, the Netherlands) with standard protocol including sagittal cuts for L1–L4 vertebra using T_1 weighted spine-echo sequence (TSE, repetition time = 400 ms, echo time = 16 ms, squared field of view = $160 \times 304 \times 48$ mm, slice thickness = 4 mm). Signals were measured by placing region of interest (ROI) in areas of the vertebral body, other than cortical bone, areas with subchondral abnormalities, posterior venous plexus and focal lesions like hemangiomas in three different sagittal slices.¹⁴ For each vertebra, three ROIs were used and their mean was used for analysis. Different ROIs were in the same size. Noise was measured in each patient in a ROI sited in a region without artifact out of the patient's body (Figure 1). SNR was calculated for each vertebra and defined as the ratio of mean of intravertebral signal intensity to standard deviation of noise. Then for each patient, the median value of vertebral bodies SNRs from L1 to L4 was calculated and named SNR_{L1-L4}. Images analysis was done by two expert radiologists who were blinded to the DXA results and are shown in Figure 1.

The same measurements were done in females aged 20–29 years.

Figure 1. T_1 weighted MRI of lumbar vertebrae measuring signal intensity in L1–L4 spines (A) and noise outside of the spine (B).

T_1 weighted images were also evaluated for compression fractures based on vertebral body height according to Genant visual semi-quantitative method.¹⁶ The terms mild, moderate, and severe compression fracture were used for loss of vertebral height less than 25%, between 25 and 40%, and more than 40% respectively based on the mentioned method. Particularly mild to moderate fractures (less than 40% loss of height) and severe fracture (more than 40% loss of height) were counted.

DXA

DXA examinations were done by using the DXA device (Hologic Discovery wi #86189) in the supine position. BMDs of lumbar vertebrae (L1–L4) were automatically obtained and BMD values were calculated using T-score.

T-score and the number of standard deviations differences from the mean for a healthy young adult, were calculated.¹⁷ Those with T-score ≥ -1 had no osteoporosis. T-score between -1 and -2.5 and T-score ≤ -2.5 were defined as osteopenia and osteoporosis respectively according to the criteria of World Health Organization.² Images of DXA examination investigating BMD and T-score are shown in Figure 2.

Data analysis

Spearman correlation analysis was used to detect the relationship between SNR_{L1-L4} and L1–L4 BMD.

Receiver operator characteristic (ROC) analysis was used to estimate the diagnostic performance of SNR_{L1-L4} using lumbar vertebral DXA as reference. Thresholds of SNR were calculated with near 90% sensitivity and specificity.

MRI-based score called M-score was calculated based on calculation formula of T-score, using SNR_{L1-L4}, mean of SNR_{L1-L4}

Figure 2. T-score and BMD of a patient measured by dual energy X-ray absorptiometry. BMD, bone mass density.

in the reference group (SNR_{Ref}) and standard deviation in the reference group (SD_{Ref}).

M-Score was calculated as follows:

$$M - Score = \frac{SNR (L1-L4) - SNR (Ref)}{SD (Ref)} \quad (1)$$

Simple correlation analysis was performed using M-score with T-score and BMD.

L1-L4 T-score was used as reference to estimate diagnostic performance of M-score using ROC analysis. For further analysis, patients were divided into two groups based on their T-score. Those with T-score ≤ -2.5 were considered as osteoporotic patients and others as non-osteoporotic. Cutoff point of M-score based on T-score method was calculated with near 90% sensitivity and specificity for distinguishing osteoporotic from non-osteoporotic patients.

All data analysis was done using SPSS (SPSS Inc., Chicago, IL, USA).

RESULTS

Descriptive statistics

The mean ages of patients were 59.1 and 26.1 years in the case and reference groups respectively. The mean weight and BMI in menopausal females were 70.69 kg and 29.87 kg/m² respectively. Among them, 10 patients (12.5 %) had normal BMI, 33 patients (40.5 %) were overweight and 39 (47%) of them were obese. Also 49 (35%) were osteoporotic, 16 (19.4 %) had osteopenia and 37 (44.5 %) had normal BMD. The mean of T-scores was -1.46 (-4.4, 0.2).

Correlation between T-score and BMD was statistically significant using Spearman correlation coefficient ($r = 0.943$). Thresholds of BMD using T-score were calculated and the following results were obtained: BMD > 0.93 was defined as normal, $0.87 < BMD < 0.93$ as osteopenia and BMD < 0.78 as osteoporotic.

Analysis of SNR

The median value of signals for each vertebra in the case group was 214.91 (129.6–323) in L1, 221.89 (131–328) in L2, 222.1 (122–325) in L3 and 218.15 (129–325) in L4 vertebra. It was 167.23 (108–242), 161.93 (103–230), 163.57 (104–271) and 158.92 (100–242) in L1–L4 vertebrae, respectively in the reference group. Noise ranged from 0 to 4.6.

The mean was 256.88 (154, 379.5) for SNR $L1-L4$ in post-menopausal females.

The Spearman correlation coefficient analysis showed a statistical correlation between SNR and BMD ($r = -0.564$, $p < 0.001$). Diagnostic ranges of SNR obtained by Spearman correlation coefficient were as follows: SNR < 238.49 as normal BMD, 238.49–271.325 as osteopenia and ≥ 271.325 as osteoporosis.

BMD was used as a gold-standard for estimating the diagnostic performance of SNR using ROC analysis to detect osteoporotic from non-osteoporotic individuals. The thresholds of SNR 267.7627 with near 90% sensitivity and 260.444 when setting near 90% specificity were found. The area under the curve (AUC) was 0.99 [95% confidence interval (CI) (0.975–1.000)] (Figure 3).

Analysis of M-score

Mean of M-scores was 1.76 (-0.9, 4.94) in post-menopausal females.

M-score was negatively correlated with T-score ($r = -0.551$, $p = 0.0001$). M-score values obtained using Spearman correlation were M-score < 1.26 for normal density, $1.26 \leq M\text{-score} \leq 2.05$ for osteopenia and M-score > 2.05 for osteoporosis (Table 1). AUC at ROC analysis for M-score based on T-score as gold standard (T-score < -2.5 for osteoporosis and -2.5 to -1 for osteopenia) was 0.92 (95% CI: 0.866–0.978) (Figure 3). The cutoff points of 1.96 for M-score with a sensitivity of near 90% (83% specificity) and 2.33 with a specificity of near 86% (76% sensitivity) were found for distinguishing osteoporotic from non-osteoporotic individuals.

Based on M-score 46.3% of post-menopausal females had normal BMD. Osteopenia was detected in 15.9 and 37.8% were osteoporotic.

Fractures

71 females (86.58%) had no fracture in MRI. Mild to moderate fracture was seen in 10 patients (12.2%). Severe fracture was diagnosed in one female. In menopausal females with mild to moderate fracture, or with no fracture mean of T-scores was -0.24 and -1.68 respectively.

Figure 3. ROC curve for M-score (left) and SNR (right) for distinguishing osteoporotic from non-osteoporotic individuals. ROC, receiver operator characteristic; SNR, signal-to-noise ratio.

Using T-score, among the 10 patients with mild to moderate fracture, 50% were osteoporotic and 20% had osteopenia.

According to M-score values, 1 of 10 (10%) patients with mild to moderate fracture was osteoporotic, 6 (60%) had osteopenia and 3 (30%) had normal BMD. Mean value of M-scores was 1.48 in patients with mild to moderate fractures and 1.81 in those without fracture.

DISCUSSION

Despite the high rate of osteoporosis and fragility fractures, small number of DXA examinations are done in high risk patients.^{14,18} Another problem with screening of osteoporosis with T-score measuring is an increase of lumbar BMD measured by DXA examination in patients with obesity and degenerative joint disease (DJD), and false assurance of low fracture risk in these patients, while M-score is not affected by BMI ≥ 30 and DJD.^{14,19} Due to high prevalence of low back pain, rate of routine lumbar MRI is increasing. Using the new quantitative MRI method based on T-score (M-score) and SNR in patients that have undergone routine MRI can help physicians to detect patients at risk of osteoporosis and can be used as an opportunistic screening method.¹⁴

Table 1. Diagnostic performance of M-score and SNR_{L1-L4} for detecting osteoporotic from non-osteoporotic females

	M-score	SNR
AUC with 95% CI	0.922 (0.866–0.978)	0.990 (0.975–1.000)
Cutoff point	2.05	271.325
Sensitivity	90%	80.7%
Specificity	87%	84.9%
NPV	93.8%	90%
PPV	78.8%	72.41%

AUC, area under the curve; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; SNR, signal-to-noise ratio.

M-score is a device-dependent score and is different in multiple devices. Considering the lack of M-score cut-off point for detecting osteoporosis using Ingenia, Philips MRI devices in Iranian society, the relationship between T-score and M-score was investigated and thresholds of M-score and SNR were found in detecting osteoporotic individuals using MRI device which is a step towards reducing the complications of osteoporosis.

Investigation of the correlation between SNR_{L1-L4} and BMD in this study showed an increase of SNR with decrease of BMD which is similar to the study of Bandirali *et al*.¹⁴ Bandirali *et al* calculated the SNR_{L1-L4} cut-off point of 36 when setting near 90% sensitivity and 51 when setting near 90% specificity for distinguishing between osteoporotic and non-osteoporotic individuals.¹⁴ In this study, we found the threshold of SNR <238.49 as normal, 238.49–271.325 as osteopenia and ≥ 271.325 as osteoporosis based on BMD.

Different result for SNR and BMD may be obtained using different calibrated instruments. To reduce the variations, M-score and T-score were introduced to consider MRI and DXA examination respectively.^{14,19} In analyzing the correlation between M-score and T-score in this study, an increase of M-score was seen with decreasing of T-score. This negative correlation was also reported in the previous study.¹⁴

The previous study showed that the M-score threshold of 5.5 can be used as a reference standard for detecting osteoporotic patients with sensitivity near 54 and 90% specificity.¹⁴ In this study on 83 post-menopausal females, the cut-off point for M-score was 2.05 for distinguishing osteoporotic patients from non-osteoporotic individuals with a sensitivity of near 90%, specificity of near 87%, positive predictive value of 78.8% and negative predictive value of 93.8%. Also M-score <1.26 showed normal bone density and $1.26 \leq \text{M-score} \leq 2.05$ was considered as osteopenia. Different results are due to different MR systems used in two studies. Also it should be noted that while AUC's are independent statistics, sensitivity, specificity, negative predictive value and positive

predictive value are data dependent and those reported in recent study are optimized for M-scores obtained in our setting and different results may be reported in other settings.

In this study, 37.8% of post-menopausal females were osteoporotic using M-score as compared to 35%, applying T-score.

One of our study's limitation is the small sample size which made some statistical analysis impossible. Another limitation is that in this study, females in the reference group did not undergo DXA and were considered as healthy and non-osteoporotic people.

Despite the mentioned limitations, this study was a prospective study which introduced MRI as an opportunistic test in detecting high risk patients for osteoporosis. Also due to MRI device-dependent values of SNR, the cut-off point of M-score for MR system of Ingenia, Philips was built. Since images obtained

by MRI devices are largely dependent on building structures and equipments in external field and homogeneity of magnetic field, the obtained cut-off points for SNR and M-score are not validated for all Ingenia, Philips 1.5 T MRI devices. They can be measured for each device specifically using the method mentioned in this study and previous studies. Based on this study DXA is not going to be replaced by MRI and it still remained gold-standard and the best method in diagnosis of osteoporosis, BMD testing and monitoring body response to osteoporotic drugs.²⁰

ACKNOWLEDGMENT

This project was thesis of Maede Khodayi (resident of radiology in Isfahan University of Medical Sciences). We would like to show our gratitude to our colleague Amir Hossein Sarrami from Department of radiology, Isfahan University of Medical Sciences, Isfahan, Iran for his comments on early version of the manuscript.

REFERENCES

1. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int* 2014; **25**: 2359–81. doi: <https://doi.org/10.1007/s00198-014-2794-2>
2. Organization WH. *Prevention and management of osteoporosis: report of a WHO scientific group*: World Health Organization; 2003.
3. Cauley JA, Lui LY, Ensrud KE, Zmuda JM, Stone KL, Hochberg MC, et al. Bone mineral density and the risk of incident nonspinal fractures in black and white women. *JAMA* 2005; **293**: 2102–8. doi: <https://doi.org/10.1001/jama.293.17.2102>
4. Kanis JA, Delmas P, Burckhardt P, Cooper C, Torgerson D, Do T. Guidelines for diagnosis and management of osteoporosis. *Osteoporosis International* 1997; **7**: 390–406. doi: <https://doi.org/10.1007/BF01623782>
5. King AB, Fiorentino DM. Medicare payment cuts for osteoporosis testing reduced use despite tests' benefit in reducing fractures. *Health Aff* 2011; **30**: 2362–70. doi: <https://doi.org/10.1377/hlthaff.2011.0233>
6. Shen W, Chen J, Punyanitya M, Shapses S, Heshka S, Heymsfield SB. MRI-measured bone marrow adipose tissue is inversely related to DXA-measured bone mineral in Caucasian women. *Osteoporos Int* 2007; **18**: 641–7. doi: <https://doi.org/10.1007/s00198-006-0285-9>
7. Tang GY, Lv ZW, Tang RB, Liu Y, Peng YF, Li W, et al. Evaluation of MR spectroscopy and diffusion-weighted MRI in detecting bone marrow changes in postmenopausal women with osteoporosis. *Clin Radiol* 2010; **65**: 377–81. doi: <https://doi.org/10.1016/j.crad.2009.12.011>
8. Yeung DK, Griffith JE, Antonio GE, Lee FK, Woo J, Leung PC. Osteoporosis is associated with increased marrow fat content and decreased marrow fat unsaturation: a proton MR spectroscopy study. *J Magn Reson Imaging* 2005; **22**: 279–85. doi: <https://doi.org/10.1002/jmri.20367>
9. Griffith JE, Yeung DK, Antonio GE, Wong SY, Kwok TC, Woo J, et al. Vertebral marrow fat content and diffusion and perfusion indexes in women with varying bone density: Mr evaluation. *Radiology* 2006; **241**: 831–8. doi: <https://doi.org/10.1148/radiol.2413051858>
10. Schellinger D, Lin CS, Hatipoglu HG, Fertikh D. Potential value of vertebral proton MR spectroscopy in determining bone weakness. *AJNR Am J Neuroradiol* 2001; **22**: 1620–7.
11. Shah LM, Hanrahan CJ. MRI of spinal bone marrow: Part I, techniques and normal age-related appearances. *AJR Am J Roentgenol* 2011; **197**: 1298–308. doi: <https://doi.org/10.2214/AJR.11.7005>
12. Abate N, Burns D, Peshock RM, Garg A, Grundy SM. Estimation of adipose tissue mass by magnetic resonance imaging: validation against dissection in human cadavers. *J Lipid Res* 1994; **35**: 1490–6.
13. Shen W, Scherzer R, Gantz M, Chen J, Punyanitya M, Lewis CE, et al. Relationship between MRI-measured bone marrow adipose tissue and hip and spine bone mineral density in African-American and Caucasian participants: the CARDIA study. *J Clin Endocrinol Metab* 2012; **97**: 1337–46. doi: <https://doi.org/10.1210/jc.2011-2605>
14. Bandirali M, Di Leo G, Papini GD, Messina C, Sconfienza LM, Ulivieri FM, et al. A new diagnostic score to detect osteoporosis in patients undergoing lumbar spine MRI. *Eur Radiol* 2015; **25**: 2951–9. doi: <https://doi.org/10.1007/s00330-015-3699-y>
15. Densitometry ISfC, Densitometry ISfC. ISCD official positions: adult. *ISCD Middletown* 2013; **2015**.
16. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res* 1993; **8**: 1137–48. doi: <https://doi.org/10.1002/jbmr.5650080915>
17. Schousboe JT, Shepherd JA, Bilezikian JP, Baim S. Executive summary of the 2013 International Society for clinical densitometry position development conference on bone densitometry. *J Clin Densitom* 2013; **16**: 455–66. doi: <https://doi.org/10.1016/j.jocd.2013.08.004>
18. Elliot-Gibson V, Bogoch ER, Jamal SA, Beaton DE. Practice patterns in the diagnosis and treatment of osteoporosis after a fragility fracture: a systematic review. *Osteoporos Int* 2004; **15**: 767–78. doi: <https://doi.org/10.1007/s00198-004-1675-5>
19. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. *The Lancet* 2002; **359**: 1929–36. doi: [https://doi.org/10.1016/S0140-6736\(02\)08761-5](https://doi.org/10.1016/S0140-6736(02)08761-5)
20. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ* 1996; **312**: 1254–9. doi: <https://doi.org/10.1136/bmj.312.7041.1254>