Feasibility of using double-echo chemical shift imaging to monitor bone mass change in aged patients with lumbago: a pilot study

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Abstract

Background: For aged patients with lumbago, monitoring bone mass change is of great importance for the early diagnosis of osteoporosis. The present study aimed to evaluate the feasibility of using the double-echo chemical shift imaging (CSI) to detect bone mass change in aged population with lumbago. We calculated chemical shift rate (CSR) from double-echo CSI data, and investigated whether CSR correlate to bone mass change. **Methods:** Two-hundred patients (aged from 60 to 70) with lumbago were included in the study. Each subject accepted a lumbar MR examination, for which the ordinary spin echo T1-Weighted sequence was modified to the double-echo imaging. By doing so, in-phase and out-phase images could be obtained simultaneously with one acquisition. The bone mineral density (BMD) was measured with digital X-ray radiogrammetry (DXR) at the non-dominant hand. Then all subjects were grouped according to their T-value (normal bone mass group, T-value > -1.0; abnormal bone mass group T-value $\leq$ -1.0). The CSR were calculated based on the signal intensity (SI) measured respectively at the 3rd – 5th lumbar vertebrae. The association of CSR with BMD was investigated, as well as the impact of other factors on BMD. **Results:** Patients with normal and abnormal bone mass showed significant difference in CSR ($P = 0.008$), that positively correlated with T-value ($r = 0.281$, $P \leq 0.001$) and negatively correlated with the diagnosis of abnormal bone mass ($B = -3.02$, $P = 0.010$). Furthermore, the risk of abnormal bone mass increased by 4.9% for each unit decrease in CSR. Additionally, females were more likely to have abnormal bone mass than males ($P = 0.017$), while the patients who had type 2 diabetes was determined to undergo 3.25-time risk to have abnormal bone mass, compared to those who did not have. **Conclusions:** CSR could be used to predict the bone mass loss in elderly patients with lumbago. Our study provides a more economical solution to monitor bone mass lose in elderly patients who complained lumbago and required lumbar MR imaging. And among such patients, the double-echo CSI is highly recommended to those who have type 2 diabetes.

Background

Osteoporosis is able to cause lumbago in the elderly population and, more importantly, poses high risk of fragility fractures secondary to fall [1]. The incidence of osteoporosis rises due to the increasing number of aged individuals. The severity of bone loss ranges from milder degrees of bone loss, termed osteopenia, to more profound degrees of loss resulting in osteoporosis [2]. Osteopenia is a condition that the bone density is reduced before it can be diagnosed as osteoporosis. Although osteopenia has no sign or symptom, medication is still suggested to prevent it deteriorates into osteoporosis. Therefore, monitoring bone mass change in aged population is of great importance for timely diagnosis and management.

Currently, dual-energy X-ray absorptiometry (DXA) is the standard method used for diagnosis of osteoporosis, evaluating fracture risk and efficacy follow-up [3]. However, DXA is not widely equipped in clinics due to its high cost and requirement for professional staff [4-6]. On the other hand, digital X-ray radiogrammetry (DXR) is used to estimate the bone mineral density (BMD) from standard hand X-ray

images [7], and to predict osteoporosis. The advantage of DXR is that it has the same accuracy as DXA [8, 9], but a faster and simpler procedure.

Bone marrow fat (BMF) content is an indicator of bone mass change [10, 11]. Increase in BMF content changes some features of bone, such as marrow fat content is inverse correlation to the amounts of cortical bone, and greater marrow fat content reduced cancellous bone density [12, 13]. Increased BMF was found in subjects with osteoporosis compared to subjects with osteopenia and normal bone mass [14]. The inverse association between BMD and BMF may lead to bone mass change and eventually lead to bone weakness. The vertebral BMF content is considered as an indicator for evaluating osteoporosis-related fracture risk, particularly in patients with diabetes where BMD measurements are limited in their ability to predict bone mass [15].

The BMF content is routinely quantitated by the double-echo chemical shift imaging (CSI), which is able to reflect the chemical shift effect between free water protons and lipid protons in human tissues through the in-phase and out-phase images [16, 17]. The degree of signal decline between the out-phase image and the in-phase image, namely chemical shift rate (CSR), is calculated to determine the BMF content. Better than DXA and CT, MRI enables both qualitative and quantitative evaluation without ionizing radiation [18, 19]. Despite the double-echo CSI is commonly used in abdominal scan [20], but its application in evaluating the fat content in bone marrow still needs more work.

The aim of this study was to use double-echo CSI to calculate CSR of lumbar in aged patients with lumbago, to evaluate the feasibility of double-echo CSI in detecting bone mass change and the correlation between CSR and BMD.

Methods

Patients

Two-hundred patients from the health service center of Shanghai Hudong community were included. There were 100 females and 100 males aged from 60 to 70, and all of them went to the hospital for BMD measurement and lumbar MRI imaging because of lumbago without trauma. Those who have a history of spinal deformity, bone tumor, lumbar tuberculosis or other metabolic bone disease were excluded. The study was conducted under the supervision of the Ethic Committee of Tongji University and informed consent from all subjects were obtained.

Patients were arranged randomly to two different groups according to their BMD values (T-value): normal bone mass group, T-value > -1.0 ; abnormal bone mass group including low bone mass ($-2.5 < \text{T-value} \leq -1.0$) and osteoporosis (T-value ≤ -2.5). Other clinical information were collected including age, gender, history of type 2 diabetes, body mass index (BMI), total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL).

Imaging

Each subject accepted lumbar MR scan on a 3.0 Tesla MRI (Philip Achieva), with the setting as: repetition time = 180ms, 1st echo time = 1.15ms, 2nd echo time = 2.3ms, slice thickness = 1.5mm, gathering matrix = 140 × 185 pixels, reconstruction matrix = 224 × 224 pixels. The conventional sagittal T1-Weighted (T1-WI) imaging was replaced with the double-echo CSI, whereby the in-phase and out-phase images can be obtained simultaneously.

The BMD data of all patients were obtained from the Carestream DXR machine (model number: DRX-NOVA, ShangHai, China). DXR estimated BMD of patients' non-dominant hand in a standard hand radiograph [7]. In particular, the patient's non-dominant hand was placed on the aluminum wedge template with the palm facing down, fingers should be positioned as shown in Figure 1(a). Then an X-ray image was obtained the original digital image is sent to BMD software (Kodak BMD System 2.0). At the same time, the gender, age, race and other information of patients were inputted. Eventually, the T-value was automatically generated by referring to the database of normal people (Fig. 1). The aluminum wedge is used to compensate the influence of voltage, exposure time and other possible unstable factors on BMD and ensure the reliability of the results.

Image analysis

MR images were anonymized and assessed independently by a senior consultant radiologist. Particularly, the quadrate regions of interest (ROIs) were placed on the 3rd – 5th lumbar vertebrae by covering vertebral corpus without cortex. Meanwhile, the psoas major muscle around the vertebrae was taken as the reference. The signal intensity (SI) values was measured both on in-phase and out-phase chemical shift images on the middle sagittal plane of the lumbar vertebrae (Fig. 2). The relative signal intensity of lumbar vertebrae and CSR values were calculated through the formulae: $SI = SI_{\text{vertebrae}} / SI_{\text{muscle}}$; CSR of lumbar vertebrae: $R_c = (SI_{IP} - SI_{OP}) / SI_{IP}$. (In the equations, SI_{IP} represents the relative SI of lumbar vertebrae in in-phase; SI_{OP} represents the relative SI of lumbar vertebrae in out-phase).

Statistical methods

All statistical analyses were performed using the SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). Data were reported as mean ± standard deviation (SD). CSR was statistically compared based on BMD measurements results between normal and abnormal bone mass group.

The correlation between CSR and BMD value (T-value) was tested by Spearman analysis. In univariate analysis, comparison of CSR between two groups

was done with independent sample T-test. In multivariate analysis, we employed binary logistic regression to analyze predictive factors of bone mass change and to evaluate whether CSR is an independent predictor. For all statistical results, $P < 0.05$ was considered statistically significant.

Results

Patient demography

The basic information of 200 patients are listed in Table 1. There were two-hundred patients including 100 females (50.0 %) and 100 males (50.0 %), aged from 60 to 70. Among those 132 (66.0 %) patients had history of type 2 diabetes. Eighty-one (40.5 %) patients were of normal BMI. The mean CSR was 0.597 ± 0.144 (range, 0.036 - 0.823), the mean TC was 4.868 ± 0.998 (range, 2.400 - 9.800 mmol/L), the mean TG was 1.718 ± 1.078 (range, 0.480 - 9.870 mmol/L), the mean HDL was 1.206 ± 0.378 (range, 0.700 - 4.720 mmol/L) and the mean LDL was 3.159 ± 0.874 (range, 0.340 - 6.420 mmol/L).

Table 1 Basic information of 200 patients

Variable	Total (n=200)	Normal (n=68)	Abnormal (n=132)	P
Age (years)				
≤65	50.0% (100)	58.8% (40)	45.5% (60)	0.073
≥65	50.0% (100)	41.2% (28)	54.5% (72)	
Gender				
Male	50.0% (100)	61.8% (42)	43.9% (58)	0.017
Female	50.0% (100)	38.2% (26)	56.1% (74)	
M-CSR	0.597 ± 0.144	0.634 ± 0.136	0.578 ± 0.145	0.008
Type 2 diabetes				
Yes	66.0% (132)	76.5% (52)	60.6% (80)	0.025
No	34.0% (68)	23.5% (16)	39.4% (52)	
BMI (kg/m ²)				
≤24	40.5% (81)	42.6% (29)	39.4% (52)	0.657
≥24	59.5% (119)	57.4% (39)	60.6% (80)	
TC (mmol/L)	4.868 ± 0.998	4.957 ± 1.026	4.823 ± 0.984	0.369
TG (mmol/L)	1.718 ± 1.078	1.682 ± 0.972	1.737 ± 1.131	0.734
HDL (mmol/L)	1.206 ± 0.378	1.197 ± 0.297	1.211 ± 0.415	0.802
LDL (mmol/L)	3.159 ± 0.874	3.293 ± 0.916	3.090 ± 0.848	0.122

M-CSR: Mean value of CSR of lumbar 3rd - 5th vertebrae; BMI: body mass index; TC: total cholesterol; TG: triglyceride; HDL: high density lipoprotein; LDL: low density lipoprotein

Correlation analysis between CSR and bone mass change

There was a statistically significant difference in CSR between normal and abnormal bone mass ($P = 0.008$). Spearman analysis showed that CSR was positively correlated with T-value ($r = 0.281$, $P \leq 0.001$) (Fig. 3), the CSR of normal bone mass group was higher than that of abnormal bone mass group. The mean CSR of the third lumbar vertebra was significantly higher in normal bone mass group of 0.649 compared to abnormal bone mass group, 0.592 ($P = 0.009$); the mean CSR of the fourth lumbar vertebra was significantly higher in normal bone mass group of 0.633 compared to abnormal bone mass group, 0.579 ($P = 0.015$); the mean CSR of the fifth lumbar vertebra was significantly higher in normal bone mass group of 0.621 compared to abnormal bone mass group, 0.563 ($P = 0.015$) (Fig. 4).

Correlation analysis between other factors and bone mass change

According to the group with or without type 2 diabetes history, the difference in bone mass between the two groups was statistically significant ($P = 0.025$), patients with a history of type 2 diabetes are more easily to have abnormal bone mass. There was a statistically significant difference in bone mass between the two groups of different genders ($P = 0.017$), and females are more prone to have abnormal bone mass than males. There were no statistically significant differences in age, BMI, TC, TG, HDL and LDL between the two groups.

Multivariate Analysis of Predictors of Bone Mass Change

We undertook a multivariate analysis, including CSR, gender, history of type 2 diabetes because CSR was correlated with bone mass change (Table 2). The results show that CSR was an independent predictor of abnormal bone mass ($P = 0.010$), CSR was negatively correlated with the diagnosis of abnormal bone mass ($B = - 3.02$), and the risk of abnormal bone mass increased by 4.9% for each unit decrease in CSR. The history of type 2 diabetes also was correlated independently with abnormal bone mass ($P \leq 0.001$), the patients who had type 2 diabetes was determined to undergo 3.25-time risk to have abnormal bone mass, compared to those who did not have.

Table 2 Independent predictors of Bone Mass Change

Variable	B	OR	95 % CI	P
CSR	-3.016	0.049	0.005-0.486	0.010
Type 2 diabetes	1.179	3.250	0.245-0.916	≤ 0.001

B, regression coefficient; OR, odds ratio; CI, confidence interval.

Discussion

Osteoporosis is a metabolic disease that bone fragility increases due to bone mass loss and osseous structure change [21]. Osteoporosis posts a great concern since it is often associated with lumbago that brings disability to who suffer from it and huge socioeconomic burden to the healthcare system. Unfortunately, osteoporosis has recently become increasingly common since the population grows old as the birth rate slowing down [22]. The osteoporosis usually is known when a bone fracture occurs to the patient secondary to a low-energy trauma, for example, a fall from ground. And the risk of fragility fracture often depends on bone mass, as well as BMD. Specifically, fractures at femur neck and distal radius present two common types of fractures in the aged people with osteoporosis, and the reason can largely attribute to that osteoporosis is not diagnosed timely and thus no treatment is given.

Osteopenia, the early stage of bone mass loss, could be prevented from developing into its subsequent stage, osteoporosis, by changing lifestyle such as balanced diet and exercise. Therefore, trying to notify bone mass loss at its early stage is of great clinical relevance that reduce the risk of osteoporosis associated bone fractures.

The BMF content can be used as a predictor of bone mass change. Previous studies [23-25] proved that the alternation in bone marrow composition of vertebra that characterized by decreased BMD and increased BMF content was strongly correlated with osteoporosis. Furthermore, a study in healthy adults had demonstrated a significantly negative correlation between the BMF content and the BMD value [10, 11]. Studies by Griffith et al. [26, 27] showed the similar finding that the patients with osteoporosis possessed significantly higher BMF content than the healthy individuals.

Double-echo CSI used in the present study holds advantages in measuring BMF content, comparing to the magnetic resonance spectroscopy (MRS) previously used by many studies [27-29]. Although MRS can precisely detect the fat content in the minor volume of tissue [30], however, its application in measuring BMF content is limited because it has low spatial resolution and fat is not evenly distributed within the bone marrow [31, 32]. The double-echo CSI has the advantages of higher spatial resolution, which is valuable especially in areas with heterogeneous marrow fat distribution that can overcome such limitation [32].

In accordance with present study, we demonstrated patients who had lower BMD values (abnormal bone mass group) obtained significantly lower CSR values (0.578 ± 0.145 vs. 0.634 ± 0.136 , $P = 0.008$), suggesting higher BMF content in the lumbar vertebrae. And, we also found the positive correlation between the CSR value and the T-value. These findings inclusively allow using the CSR value to predict osteoporosis in aged patients with lumbago. To note, Gokhan G et al. [33] claimed that the vertebral BMF content calculated from chemical-shift MRI is not reliable for predicting BMD in female patients aged between 50 and 65 years. The difference between their work and our study could be explained from two aspects: one is our study included both males and females but the subjects of them were only females; another one is the subjects in our study had a varied interval of age (aged from 60 to 70), and the median age of subjects in our study was 65.5 but that of their work was 55.9.

The relationship between diabetes and osteoporosis has been consistently confirmed. Increasing evidences support the association between type 2 diabetes increased fracture risk [34, 35]. Diabetic osteoporosis refers to metabolic bone disease secondary to diabetes mellitus, including bone loss, bone microstructure damage, bone brittleness increases and fracture-prone [36]. The present study verified that patients with a history of type 2 diabetes were more easily to have bone mass change ($P \leq 0.001$), and such finding is corroborative with previous studies [37, 38]. Furthermore, the risk of fracture increases with the progressing type 2 diabetes [39]. Therefore, early monitoring of bone mass change in patients with diabetes is needful for timely and effective clinical intervention.

The vertebral BMF content increases sharply in postmenopausal females [40]. Although both androgen and estrogen levels fall in later years, estrogen levels decline particularly sharply in postmenopausal

females, which promotes greater fat deposition [41]. Females over 65 years have 10% greater BMF content than males even for the same age [42]. The pathogenesis of osteoporosis in postmenopausal females is closely related to the reduction of estrogen levels [43]. The decrease of estrogen levels weakens the excitability and activity of osteoblasts because estrogen receptors existing on the surface of osteoblasts [44]. Hence, the dynamic balance between osteoblasts and osteoclasts is lost, and the reabsorption capacity of osteoclasts is enhanced, resulting in bone loss. Females of the present study were postmenopausal, and the results showed that females were more prone to have abnormal bone mass than males.

BMF content is continuously increasing with age [45, 46]. BMF in the vertebrae body is approximately 20-25% in the 11-20-year group and rises to 65-75% in the 81-90-year group [45]. Nevertheless, our study found no association between the bone mass change and age. This difference can be explained as the present pilot study included the subjects aged from 60 to 70, no younger subjects were enrolled for comparison. Age-related bone loss indicates the risk of fragility fracture in the aged population. Double-echo CSI can provide a more economical way to detect bone mass change, which is beneficial for early treatment in aged patients to prevent the occurrence of osteoporosis-related fractures.

This study still holds many limitations. Firstly, this study consisted of only elderly patients (aged from 60 to 70) with lumbago from one community and lacked data of other age groups from broader area. A larger sample size and more age groups are intended in the subsequent study. Secondly, the present study is preliminary and had no healthy control. Hence, the findings may be generalizable only to patients with lumbago, and this should be noted when other study quote our results. Also, the BMF content was not directly measured but indirectly related by the CSR value.

Conclusions

Our study demonstrated that CSR is correlated with BMD, suggesting that double-echo CSI can be used as a preliminary screening method for bone mass change in aged population without increasing the cost and image acquisition time.

List Of Abbreviations

CSI: chemical shift imaging; CSR: chemical shift rate; T1W: ; BMD: bone mineral density; DXR: Digital X-ray radiogrammetry; SI: signal intensity; DXA: Dual-energy X-ray absorptiometry; BMF: bone marrow fat; BMI: body mass index; TC: total cholesterol; TG: triglyceride; HDL: high density lipoprotein; LDL: low density lipoprotein; ROI: region of interest; SD: standard deviation; M-CSR: mean value of CSR of lumbar 3rd – 5th vertebrae.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Review Board of Tongji University, Shanghai, P.R. China. All patients provided written informed consent prior to their inclusion within the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Dr. Zhihua Han is a member of the editorial board of BMC Musculoskeletal Disorders. Other authors declare that they have no competing interests.

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Authors' contributions

Study design: YYS, ZHH, FW, LZ; Data acquisition: FW, YYS; MR imaging acquisition: YBW; Data analysis/interpretation: YYS, BW; Statistical analysis: SYY, BW, LZ; Manuscript editing: YYS, ZHH; Manuscript revision/review: ZHH, LZ; Final approval of the version to be submitted: YYS, ZHH, FW, BW, YBW, LZ. All authors read and approved the final manuscript.

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References

1. Kim J H, Kim J I, Jang B H, et al. The Comparison of Bone Scan and MRI in Osteoporotic Compression Fractures. Asian spine journal. 2010;4(2):89-95.
2. MacKnight, John M. Osteopenia and Osteoporosis in Female Athletes. Clin Sports Med. 2017;36(4):687-702.
3. Ponti F, Guerri S, Sassi C, et al. Imaging of diabetic bone. Endocrine. 2017; 58(3):426-441.
4. Blake GM, Fogelman I. Role of dual-energy X-ray absorptiometry in the diagnosis and treatment of osteoporosis. J Clin Densitom. 2007;10(1): 102
5. Hernlund E, Svedbom A, Ivergård M, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International

- Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos*. 2013; 8(1–2):136.
6. Curtis JR, Laster A, Becker DJ, et al. The geographic availability and associated utilization of dual energy X-ray absorptiometry (DXA) testing among older persons in the United States. *Osteoporos Int*. 2009;20(9):1553–61.
 7. Kälvesten J, Lui L Y, Brismar T, et al. Digital X-ray radiogrammetry in the study of osteoporotic fractures: Comparison to dual energy X-ray absorptiometry and FRAX. *Bone*. 2016;86:30-35.
 8. Böttcher J, Pfeil A. Diagnosis of periarticular osteoporosis in rheumatoid arthritis using digital X-ray radiogrammetry. *Arthritis Res Ther*. 2008;10(1):103.
 9. Elliot JR, Fenton AJ, Young T, et al. The precision of digital X-ray radiogrammetry compared with DXA in subjects with normal bone density or osteoporosis. *J Clin Densitom*. 2005;8(2): 187–191.
 10. Shen W, Scherzer R, Gantz M, 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.
 11. Shen W, Chen J, Gantz M, Punyanitya M, Heymsfield SB, Gallagher D, Albu J, Engelson E, Kotler D, Pi-Sunyer X, Gilsanz V. MRI-measured pelvic bone marrow adipose tissue is inversely related to DXA-measured bone mineral in younger and older adults. *Eur J Clin Nutr*. 2012; 66:983-8.
 12. Wren TA, Chung SA, Dorey FJ, Bluml S, Adams GB, Gilsanz V. Bone marrow fat is inversely related to cortical bone in young and old subjects. *J Clin Endocrinol Metab*. 2011; 96(3):782-786.
 13. Griffith JF, Yeung DK, Leung JC, Kwok TC, Leung PC. Prediction of bone loss in elderly female subjects by MR perfusion imaging and spectroscopy. *Eur Radiol*. 2011; 21(6):1160-1169.
 14. Milisic, L. Vegar-Zubovic, S. Valjevac, A. Bone marrow adiposity is inversely associated with bone mineral density in postmenopausal females. *Med Glas (Zenica)*. 2020;17(1):15-21.
 15. Patsch JM, Li X, Baum T, Yap SP, Karampinos DC, Schwartz AV, et al. Bone marrow fat composition as a novel imaging biomarker in postmenopausal women with prevalent fragility fractures. *J Bone Miner Res*. 2013;28:1721–8.
 16. Karampinos DC, Yu H, Shimakawa A, Link TM, Majumdar S. T(1)-corrected fat quantification using chemical shift-based water/fat separation: application to skeletal muscle. *Magn Reson Med*. 2011;66:1312–26.
 17. Ruschke S, Pokorney A, Baum T, Eggers H, Miller JH, Hu HH, et al. Measurement of vertebral bone marrow proton density fat fraction in children using quantitative water-fat MRI. *MAGMA*. 2017;30:449–60.
 18. Baum T, Cordes C, Dieckmeyer M, Ruschke S, Franz D, Hauner H, et al. MR based assessment of body fat distribution and characteristics. *Eur J Radiol*. 2016;85:1512–8.
 19. Paccou J, Penel G, Chauveau C, Cortet B, Hardouin P. Marrow adiposity and bone: review of clinical implications. *Bone*. 2018. doi: 10.1016/j.bone.2018.02.008

20. Borra RJ, Salo S, Dean K, et al. Nonalcoholic fatty liver disease: rapid evaluation of liver fat content with in-phase and out-of-phase MR imaging. *Radiology*. 2009;250:130-136.
21. Strolka I, Toffanin R, Guglielmi G, Frolo I. Image registration in the T2* measurements of the calcaneus used to predict osteoporotic fractures. *Meas Sci Rev*. 2005;5:78–81.
22. Yeung DK, Griffith JF, 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.
23. Rosen CJ, Bouxsein ML. Mechanisms of disease: is osteoporosis the obesity of bone? *Nat Clin Pract Rheumatol*. 2006;2:35–43.
24. Sanchez-Riera L, Wilson N, Kamalaraj N, Nolla JM, Kok C, Li Y, et al. Osteoporosis and fragility fractures. *Best Pract ResClin Rheumatol*. 2010; 24:793–810.
25. Compston JE, Flahive J, Hooven FH, Anderson FA Jr, Adachi JD, Boonen S, et al. Obesity, health-care utilization, and health-related quality of life after fracture in postmenopausal women: Global Longitudinal Study of Osteoporosis in Women (GLOW). *Calcif Tissue Int*. 2014; 94:223–31.
26. Griffith JF, Yeung DK, Antonio GE, Lee FK, Hong AW, Wong SY, et al. Vertebral bone mineral density, marrow perfusion, and fat content in healthy men and men with osteoporosis: dynamic contrast-enhanced MR imaging and MR spectroscopy. *Radiology*. 2005; 236:945–51.
27. Griffith JF, 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.
28. Singhal V, Bredella MA. Marrow adipose tissue imaging in humans. *Bone*. 2019; 118:69–76.
29. Li X, Kuo D, Schafer AL, Porzig A, Link TM, Black D, Schwartz AV. Quantification of vertebral bone marrow fat content using 3 Tesla MR spectroscopy: reproducibility, vertebral variation, and applications in osteoporosis. *J Magn Reson Imaging*. 2011; 33:974-9.
30. Kim H, Taksali SE, Dufour S, Befroy D, Goodman TR, Petersen KF, et al. Comparative MR study of hepatic fat quantification using single-voxel proton spectroscopy, two-point dixon and three-point IDEAL. *Magn Reson Med*. 2008;59(3):521–7.
31. Nouh MR, Eid AF. Magnetic resonance imaging of the spinal marrow: Basic understanding of the normal marrow pattern and its variant. *World J Radiol*. 2015; 7:448–58.
32. Li X, Schwartz AV. MRI Assessment of Bone Marrow Composition in Osteoporosis. *Curr Osteoporos Rep*. doi: 10.1007/s11914-020-00562-x.
33. Gokalp G, Mutlu F S, Yazici Z, et al. Evaluation of vertebral bone marrow fat content by chemical-shift MRI in osteoporosis. *Skeletal Radiology*. 2011; 40(5):577-585.
34. Schwartz AV, Vittinghoff E, Bauer DC, et al. Study of Osteoporotic Fractures (SOF) Research Group; Osteoporotic Fractures in Men (MrOS) Research Group; Health, Aging, and Body Composition (Health ABC) Research Group. Association of BMD and FRAX score with risk of fracture in older adults with type 2 diabetes. *JAMA*. 2011;305:2184–2192.

35. Ma L, Oei L, Jiang L, et al. Association between bone mineral density and type 2 diabetes mellitus: a meta-analysis of observational studies. *Eur J Epidemiol.* 2012;27:319–332.
36. De Paula FJA, Horowitz MC, Rosen CJ. Novel insights into the relationship between diabetes and osteoporosis. *Diabetes Metab Res Rev.* 2010;26: 622-630.
37. Janghorbani, M.; Van Dam, R.M.; Willett, W.C.; Hu, F.B. Systematic review of type 1 and type 2 diabetes mellitus and risk of fracture. *Am. J. Epidemiol.* 2007;166:495–505.
38. Fan Y, Wei F, Lang Y, Liu Y. Diabetes mellitus and risk of hip fractures: a meta-analysis. *Osteoporos. Int.* 2015;27(1): 219–228.
39. Janghorbani M, Feskanich D, Willett W C, et al. Prospective Study of Diabetes and Risk of Hip Fracture: The Nurses' Health Study[J]. *Diabetes Care.* 2006;29(7):1573-1578.
40. Kugel H, Jung C, Schulte O, Heindel W. Age- and sex-specific differences in the ¹H-spectrum of vertebral bone marrow. *J Magn Reson Imaging.* 2001;13:263–268.
41. Blouin K, Boivin A, Tchernof A. Androgens and body fat distribution. *J Steroid Biochem Mol Biol.* 2008;108:272–280.
42. Griffith JF, Yeung DK, Ma HT, Leung JC, Kwok TC, Leung PC. Bone marrow fat content in the elderly: a reversal of sex difference seen in younger subjects. *J Magn Reson Imaging.* 2012;36:225–30.
43. Amarante F, Vilodre LC, Maturana MA, et al. Women with primary ovarian insufficiency have lower bone mineral density. *Med Biol Res.* 2011;44(1):78-83.
44. Bab I, Zimmer A. Cannabinoid receptors and the regulation of bone mass. *Biochemical Pharmacol.* 2008;153(2): 182-188.
45. Dieckmeyer M, Ruschke S, Cordes C, Yap SP, Kooijman H, Hauner H, Rummeny EJ, Bauer JS, Baum T, Karampinos DC. The need for T (2) correction on MRS-based vertebral bone marrow fat quantification: implications for bone marrow fat fraction age dependence. *NMR Biomed.* 2015; 28:432–9.
46. Karampinos DC, Melkus G, Baum T, Bauer JS, Rummeny EJ, Krug R. Bone marrow fat quantification in the presence of trabecular bone: initial comparison between water-fat imaging and single-voxel MRS. *Magn Reson Med.* 2014; 71:1158–65.

Figures

a**A standard hand radiograph** **b** **Figure 1**

A standard hand radiograph and the result of BMD values. (a) A standard hand X-ray image. (b) The three curves in the figure represent the range of fluctuations for the age comparison. The middle curve is the mean curve, which represents the average value in the database, and the upper and lower curves are standard deviations. The T-value corresponding to the black spot in the figure represents the bone mass of this patient.

Figure 2

MR images analysis. (a, b) Image of mid-sagittal in-phase and out-phase of lumbar. The quadrate ROIs were placed on the 3rd – 5th lumbar vertebrae by covering vertebral corpus without cortex. (c, d) Image of psoas major muscle with the quadrate ROI being placed on it.

Mean of L3-5

Figure 3

Scatterplots displaying the correlation between CSR and BMD value (T-value). The mean CSR of the three vertebrae is positively correlated with T-value.

Figure 4

Bar chart showing comparison of CSR between two groups. (a-c) The differences of CSR between two groups of 3rd – 5th lumbar vertebrae, and the CSR of normal bone mass groups were higher than that of abnormal bone mass groups.(d) The difference of the mean CSR of 3rd – 5th lumbar vertebrae between two group, and the mean CSR of normal bone mass group was higher than that of abnormal bone mass group.