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Quantitative evaluation of vertebral marrow adipose tissue in postmenopausal female using MRI chemical shift-based water–fat separation

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AIM: To investigate the feasibility of assessing vertebral marrow adipose tissue using a magnetic resonance imaging (MRI) chemical shift-based water–fat separation technique at 3 T.

MATERIAL AND METHODS: A modified Dixon technique was performed to obtain the vertebral marrow fat fraction (FF) in a study of 58 postmenopausal females (age range 49.2–77.4 years), including 24 normal bone density, 19 osteopaenia, and 15 osteoporosis as documented with dual-energy X-ray absorptiometry. The reliability of FF measurements performed by two radiologists independently was evaluated with the intraclass correlation coefficient (ICC). Ten participants were scanned twice to assess the reproducibility of FF measurements. FF values were compared between each vertebral level and between groups.

RESULTS: The mean coefficient of variation of FF measurements was 2.1%. According to the ICC, the measurements were reliable (ICC = 0.900 for normal bone density, ICC = 0.937 for osteopaenia and ICC = 0.909 for osteoporosis, $p < 0.001$ for all). There was an inverse association between mean FF at L1–L4 vertebrae and lumbar spine BMD ($r = -0.459$, $p = 0.006$), which remained significant even after controlling for confounders (age, height, and body weight). FF values at different vertebral levels were significantly correlated to each other ($r = 0.703$–0.921, $p < 0.05$ for all). There was a general trend toward increased marrow adiposity for more inferior vertebral bodies. Patients with osteopaenia and osteoporosis had a higher marrow fat content compared with normal bone mass after adjusting for confounders, although no significant differences in each vertebral level and average marrow fat content were found between the osteopaenia and osteoporosis groups.

CONCLUSION: Chemical shift-based water–fat separation enables the quantitation of vertebral marrow adiposity with excellent reproducibility, which appears to be a useful method to provide complementary information to osteoporosis-related research fields.

Introduction

Osteoporosis is a widespread disease characterized by low bone mass and structural deterioration of bone tissue, which results in bone fragility and increased fracture

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susceptibility. This disease affects approximately one in two women and one in five men over the age of 50 years, who will experience an osteoporotic fracture during their remaining lifetime.[1,2] Both the high morbidity and its common complication osteoporotic fracture load a heavy burden on society.

An increasing number of studies have shown that a reduction in bone volume has been observed in osteoporosis related to aging, menopause, anorexia nervosa, and thiazolidinedione or glucocorticoid treatment, which is accompanied by an accumulation of the marrow fat volume.[3–7] These studies suggest that marrow adipogenesis may play an important part in the pathophysiology of osteoporosis. Targeting the marrow adipose tissue could be considered as a new diagnostic and therapeutic approach for osteoporosis.[8,9] Interestingly, the marrow fat content may also be valuable in planning and monitoring treatment of other diseases, such as cancer patients receiving radiation and/or chemotherapy, Gaucher's disease, etc.[10,11] Thus, monitoring the dynamic changes of marrow adiposity is of a high clinical significance, creating a high demand for imaging methodologies, particularly those with no exposure to ionizing radiation.

Marrow adipose content can be quantified by a variety of methods such as light microscopy,[3] gas chromatography,[12] proton magnetic resonance spectroscopy (MRS),[5,13,14] and micro-computed tomography (CT).[15] However, all the above methods have their inherent limitations, such as *ex vivo* methods, greater radiation exposure, requirement for specialized analysis software, and time-consuming. Recent advances in rapid chemical-shift magnetic resonance imaging (MRI) have led to the development of a time-efficient, computationally robust, and accurate water–fat separation techniques, such as modified two-point Dixon and IDEAL (iterative decomposition with echo asymmetry and least squares estimation). The ability of chemical shift-based water–fat separation methods to accurately separate the signals from water and fat has led to increasing interest in quantifying fatty infiltration of organs in various disease conditions, such as hepatic fat, intermuscular adipose tissue, etc.[16,17] Unfortunately, there is little information regarding whether chemical shift-based water–fat separation techniques have the potential to quantify marrow fat content at the different vertebral levels in a relatively short time. Therefore, the purpose of the present study was to explore the feasibility of characterizing the marrow adipose tissue volume by a MRI chemical shift-based water–fat separation approach using a three-dimensional (3D) spoiled gradient-echo sequence at 3 T.

Materials and methods

Subjects

The study was a cross-sectional, retrospective study performed between January 2012 and December 2012. Fifty-eight postmenopausal volunteer women (aged from 49.2–77.4 years) who were referred to our department (Department of Radiology, Yueyang Hospital, Shanghai University of Traditional Chinese Medicine). for dual-energy X-ray absorptiometry (DXA) after clinical work-up were enrolled. The participants were divided into three groups: 15 osteoporotic (age 64.5 ± 8.3 years), 19 osteopaenic (age 62 ± 6.7 years), and 24 normal participants (age 58 ± 6.4 years) based on their DXA results. Each participant's medical history was collected, particularly information regarding risk factors for osteoporosis. None of the participants had current or previous use of therapies that affect bone metabolism (such as oral contraceptive pill or hormone replacement therapy, glucocorticoids, anticonvulsants, immunosuppressive medications). No participants had diagnosed or self-reported malignancy, history of chronic disease with vital organ involvement, or previous pathological fractures. Coexisting diabetes, hysterectomy, or presence of contraindications to MRI examination (such as metal implants, claustrophobia), conditions technically interfering with DXA assessment (i.e., previous spine or hip surgery) were also excluded. Similarly, participants with a history of radiotherapy or chemotherapy or those in bed rest >1 month within the 6 months before the study were excluded.

The participants' body weight and height were obtained in order to calculate the body mass index (BMI). Body weight was measured to the nearest 0.1 kg on a portable electronic beam scale, wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm using a stadiometer.

The study was approved by the local Institutional Review Board and conducted in accordance with the Committee for Human Research. All participants provided written informed consent prior to participation in the study.

Bone mineral density measurement

The areal bone mineral density (BMD) of the lumbar vertebrae (from L1–L4) on the anteroposterior projection (Prodigy Lunar, GE Healthcare, Waukesha, WI, USA) (Version enCORE 13.40.038) was used to obtain a value expressed in grams per squared centimetres (g/cm^2) as previously described.[2] In compliance with the definition of the World Health Organization, DXA results were evaluated according to the T-score, which shows the amount of bone the subject has compared to a young adult (at the age of 35 years) of the same gender with peak bone mass. Then, subjects were grouped into three categories: normal bone density defined as T-scores ≥ -1; osteopaenia as a T-score between -1 and -2.5; and osteoporosis as a T-score ≤ -2.5.

The scanner was routinely calibrated and quality control measures were followed as recommended by the manufacturer to control for possible baseline drift. All scans were acquired and read by trained technologists. The precision of the DXA methods for BMD measurements was excellent. The coefficient of variability (*CV*) for BMD measurements at the different anatomical regions was <0.98%.[2]

MRI protocol

All MRI examinations were performed using a 3 T whole-body MRI system (MAGNETOM Verio, Siemens Healthcare,