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ORIGINAL ARTICLE

Osteopenia is associated with glycemic levels and blood pressure in Chinese postmenopausal women: a cross-sectional study

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Abstract The aim of present study was to explore the relationships between osteopenia and dyslipidemia, glycemic levels or blood pressure in postmenopausal Chinese women. A total of 4080 women aged 42–85 years were enrolled in this cross-sectional study, which was nested in an ongoing longitudinal (REACTION) study. Calcaneus quantitative ultrasound (QUS) was performed and QUS *T* score was calculated to assess bone mineral density. Osteopenia was defined as a *T* score ≤ -1.0. The relationship between osteopenia and dyslipidemia, glycemic levels or blood pressure was investigated. The prevalence of osteopenia was significantly lower in subjects with systolic blood pressure (SBP) $\geq$140 mmHg, fasting blood glucose (FBG) $\geq$8.0 mmol/L, postprandial blood glucose (PBG) $\geq$15.0 mmol/L, hemoglobin A1c (HbA1C) 6.5–7.5 %, HbA1C $\geq$7.5 %. These relationships remained significant after controlling for multiple factors. Moreover, significant trend between osteopenia and SBP, FBG, PBG and HbA1C was observed in women. In contrast, no significant associations between osteopenia and diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) were found, and no significant trend relationship between osteopenia and DBP, TC, TG, HDL-C, LDL-C was found in postmenopausal Chinese women. The present study showed a relationship between SBP, FBG, PBG, HbA1C and osteopenia in postmenopausal Chinese women, while no significant relationship was observed between dyslipidemia, DBP and osteopenia, even after controlling for multiple confounding factors.

Keywords Osteopenia · Cardiovascular diseases · Diabetes · Quantitative ultrasound

Abbreviations

QUS	Calcaneus quantitative ultrasound
BMI	Body mass index
CVD	Cardiovascular disease
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
FBG	Fasting blood glucose
PBG	Postprandial blood glucose
HbA1c	Hemoglobin A1c
SBP	Systolic blood pressure
SOS	Speed of sound
BUA	Broadband ultrasound attenuation
QUI	Quantitative ultrasound index
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
OR	Odds ratio
CI	Confidence interval
TC	Total cholesterol
TG	Triglycerides

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Introduction

Osteoporosis and its related fractures are one of the major factors of disability and death in elderly people [1]. The World Health Organization (WHO) estimates that 30 % of all postmenopausal women have osteoporosis [2]. Osteoporosis in women following menopause is a major health problem that affects up to 50 % of postmenopausal women [3]. It was found that, in postmenopausal women living in Beijing, there was an almost tenfold increase in vertebral fractures rates with age from 3.9 % at ages 50–59 years to 31.2 % (21.8–40.6 %) at age 80 years and older, and among them 42 % had two or more fractures [4]. The best way to deal with osteoporosis is to find osteopenia and treat it before the disease progresses. Osteopenia, cardiovascular diseases (CVD) and diabetes are very common age-related disorders in postmenopausal women and usually coexist in the same individual with aging. Blood pressure, dyslipidemia and diabetes are risk factors for CVD and diabetes. However, the relationship between these metabolic parameters and osteopenia is still unclear. The aim of this cross-sectional study in Beijing China was to determine whether independent relationships exist between osteopenia and dyslipidemia, glycemic levels or blood pressure. A better understanding of this relation may provide new opportunities for early intervention and may, ultimately, help prevent the bone loss in postmenopausal women.

Materials and methods

Participants and measures

The present QUS study was nested in an ongoing longitudinal (REACTION) study which was designed to investigate the association of T2DM and pre-diabetes with the risk of cancer in the Chinese population, described previously [5]. All permanent residents of Jinding communities of Beijing, China, aged 40 years and older, were invited to participate. Recruitment was performed by local resident associations and was conducted in the primary health care center located at this community. All investigators received extensive training relative to the study questionnaire and outcome measures before conducting the investigation. A total of 8400 individuals were registered between March and December, 2012. A total of 4080 postmenopausal women (age range 42–85 years) were enrolled in this study and signed the informed consents (Fig. 1). The study protocol was approved by the Committee on Human Research at Rui-Jin Hospital affiliated to School of Medicine, Shanghai Jiao Tong University.

Bone status data were obtained using the quantitative ultrasound (QUS) bone densitometer at the left calcaneus. QUS (Sahara, Hologic, USA) was used to measure the following indices: speed of sound (SOS, m/s); broadband ultrasound attenuation (BUA, dB/MHz); stiffness or the quantitative ultrasound index (QUI); and *T* score. The *T* score was produced by comparing the reference database through the built-in microprocessor. All the participants were checked by the same trained physician and same device. The QUS was calibrated in accordance with the manufacturer's recommendations and before measurement each day.

Women with a *T* score of ≤ -1.0 were classified as osteopenia according to the WHO definition of osteoporosis [6]. Then participants were classified into two groups: the non-osteopenia group, defined as a *T* score of > -1.0; and the osteopenia group, defined as a *T* score of ≤ -1.0.

All participants received comprehensive examinations that included a detailed questionnaire, anthropometric measurement, a standard 75 g oral glucose tolerance test and blood collection.

The self-administered questionnaire covered history of diabetes, hypertension, cardiovascular diseases (CVD, including myocardial infraction, stoke and coronary heart disease), alcohol intake, smoking habits, physical activity. Alcohol intake was classified as either consumption nearly/more than once a week currently or not; smoking habit was defined as either smoking more once a day or not. Physical activity was defined as engaging in sports more than once a week. BMI was calculated as body weight in kilograms divided by body height in meters squared (kg/m^2).

Blood samples were collected by venipuncture. All participants received an oral glucose tolerance test and were told to fast for at least 10 h before the test. Plasma glucose, serum triglycerides (TG), total cholesterol (TC), HDL cholesterol (HDL-C) and LDL cholesterol (LDL-C) were measured using an autoanalyzer (Cobas 8000 modular analyzer series, Roche Diagnostics, Basel, Switzerland). Hemoglobin A_1C (HbA1C) was determined by high-performance liquid chromatography using the VARIANT II Hemoglobin Testing System (Tosoh Corporation, Tokyo, Japan). HbA1C was measured together in the same device.

Statistical analysis

Statistical analysis was performed using SPSS software, version 19.0 (IBM, Chicago, IL). All continuous variables are presented as mean values and standard deviation (SD). The two-sample *t* test was used to compare the differences in baseline characteristics for all continuous variables. The differences in the proportions of the characteristics of the studied subjects were tested by Chi-square test. Then DBP was divided into <80, 80–89, ≥90 mmHg; SBP into <120, 120–140, ≥140 mmHg; TC into ≤4.14 mmol/L (160 mg/dL), 4.15–5.19 mmol/L (200 mg/dL), 5.19–6.22 mmol/L (240 mg/dL), >6.22 mmol/L; TG into <1.70 mmol/L

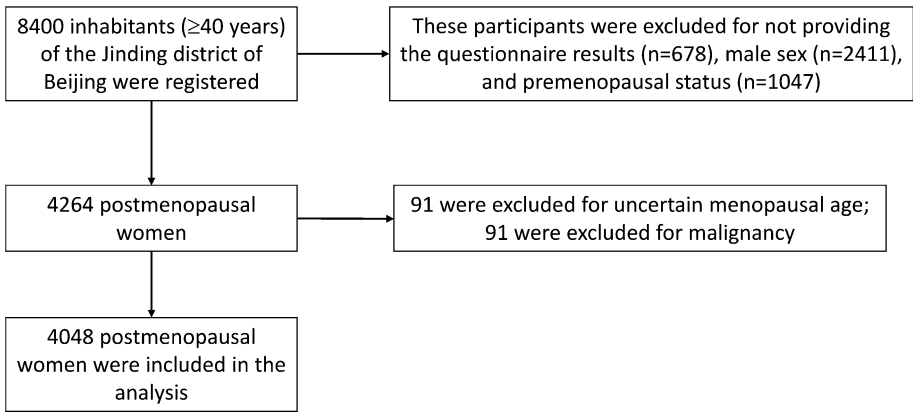

Fig. 1 Flowchart of the participant inclusion process

(150 mg/dL), 1.70–2.83, ≥2.83 mmol/L (250 mg/dL); HDL-C into <1.03 mmol/L (40 mg/dL), 1.03–1.55 mmol/L, ≥1.55 mmol/L (60 mg/dL); LDL-C into <3.37 mmol/L (130 mg/dL), 3.37–4.14, ≥4.14 mmol/L (160 mg/dL); HbA1C into <6.50, 6.50–7.50, ≥7.50 mmol/L; FPG into <6.1, 6.1–7.0, 7.0–7.9, ≥8.0 mmol/L; PPG into <11.1, 11.1–13.0 mmol/L, 13.0–14.9, ≥15.0 mmol/L. The odds ratios (ORs) with 95 % confidence intervals (CIs) for low BMD were estimated by conducting logistic regression analyses to test the relationship between low BMD and TC, LDL-C, HDL-C, TG, HbA1C, FPG, PPG, SBP, DBP (all used as categorical variables). Multiple factors were considered, including age, physical activity, smoking, alcohol consumption, menopause age and BMI. The model was adjusted for these multiple confounding factors. Reported values were the multivariable-adjusted means and 95 % CIs. In all analyses, $P < 0.05$ was considered to be statistically significant.

Ethics statement

The study was nested in an ongoing longitudinal (REACTION) study, which is supported by the Chinese Society of Endocrinology and guided by Rui-Jin Hospital affiliated to School of Medicine, Shanghai Jiao Tong University. All procedures used in this study followed the institutional guidelines. The study protocol was approved by the Committee on Human Research at Rui-Jin Hospital affiliated to School of Medicine, Shanghai Jiao Tong University, and the informed consents were given by all study participants [5].

Results

Characteristics of the study subjects are shown in Table 1. A total of 4080 postmenopausal women (age range 42–85 years) were included in this study. The prevalence of osteopenia was 69.5 %. No significant differences between women with or without osteopenia were observed in regard to WC, TC, TG, LDL-C, SBP, FPG, PPG, HbA1C, physical activity, smoking status or alcohol consumption.

The group with osteopenia comprised 11.8 % patients with CVD, 43.8 % with hypertension, 21.9 % with type 2 diabetes mellitus and 11.3 % with a history of fracture. Women with osteopenia were older at enrollment ($P < 0.001$), had lower BMI ($P < 0.001$) and DBP ($P < 0.001$), had earlier menopause age ($P < 0.001$) and had higher HDL-C ($P = 0.007$) than those without osteopenia. In addition, women with osteopenia were more likely to have CVD ($P = 0.014$), hypertension ($P = 0.034$) and a fracture history ($P < 0.001$) than those without osteopenia.

We then examined which parameters relevant to CVD and diabetes are independently associated with osteopenia. Multiple logistic regression analysis with parameters relevant to CVD (including previous diagnosis of CVD, DBP, SBP, TC, TG, HDL-C and LDL-C), diabetes (including diagnosed T2DM, FPG, PPG and HbA1C) as independent categorical variables and corrected for confounding factors (Model 1 included age at enrollment for adjustment; Model 2 included the covariate in model 1 and also physical activity, smoking, alcohol consumption, age at menopause; Model 3 included the covariates in model 2 and also BMI for adjustment) was conducted.

Tables 2 and 3 show adjusted ORs for osteopenia according to the classification of parameters relevant to CVD or diabetes. The prevalence of osteopenia was significantly lower in subjects with SBP ≥ 140 mmHg (age-adjusted OR 0.719 [95 % CI 0.593, 0.871]); FBG 7.0–7.9 mmol/L (0.659 [0.473, 0.918]); FBG ≥ 8.0 mmol/L (0.720 [0.541, 0.958]); PBG ≥ 15.0 mmol/L (0.690 [0.513, 0.926]); HbA1C 6.5–7.5 % (0.638 [0.495, 0.824]); HbA1C ≥ 7.5 % (0.715 [0.533, 0.960]). These relationships remained significant even after controlling for multiple factors (SBP ≥ 140 mmHg: multivariable-adjusted OR 0.781 [95 % CI 0.636, 0.959]; FBG 7.0–7.9 mmol/L: 0.709 [0.506, 0.994]; FBG ≥ 8.0 mmol/L: 0.726 [0.544,

Table 1 General characteristic of study participants

	Non-osteopenia group ($n = 1244$)	Osteopenia group ($n = 2836$)	P value
Age and weight variables			
Age, years	57.2 ± 5.8	59.9 ± 6.8	**<0.001**
Menopause age, years	49.6 ± 3.7	49.0 ± 3.9	**<0.001**
BMI, kg/m^2	25.6 ± 3.5	25.2 ± 3.6	**<0.001**
Waist circumference, cm	84.0 ± 9.0	83.7 ± 9.0	0.229
Characteristics relevant to CVD			
Previous diagnosis of CVD, %	9.2	11.8	**0.014**
Total cholesterol, mmol/L	5.33 ± 0.98	5.33 ± 0.97	0.861
Triglycerides, mmol/L	1.68 ± 1.16	1.61 ± 0.97	0.062
HDL-C, mmol/L	1.45 ± 0.34	1.48 ± 0.36	**0.007**
LDL-C, mmol/L	3.29 ± 0.80	3.28 ± 0.82	0.756
hypertension, %	40.2	43.8	**0.034**
SBP, mmHg	129.8 ± 16.5	129.8 ± 16.6	0.888
DBP, mmHg	75.8 ± 9.2	74.6 ± 9.0	**<0.001**
Characteristics relevant to diabetes			
Diabetes mellitus, %	22.9	21.9	0.474
FBG, mmol/L	5.79 ± 1.57	5.75 ± 1.54	0.425
PBG, mmol/L	8.53 ± 3.73	8.41 ± 3.57	0.362
HbA_{1c}	6.02 ± 1.07	5.97 ± 0.96	0.120
Lifestyle habits			
Smoking, %	0.3	0.3	0.835
Alcohol consumption, %	0.1	0.4	0.098
Physical activity, %	13.0	11.8	0.263
Characteristics relevant to osteoporosis			
History of fracture, %	7.0	11.3	<0.001
T value	−0.03 ± 0.89	−1.98 ± 0.68	<0.001
SOS, m/s	1555.4 ± 23.8	1508.1 ± 16.8	<0.001
BUA, dB/MHz	84.9 ± 12.5	58.4 ± 11.9	<0.001
QUI	101.5 ± 14.0	71.3 ± 10.7	<0.001

BMI body mass index, *CVD* cardiovascular disease, *HDL-C* HDL cholesterol, *LDL-C* LDL cholesterol, *DBP* diastolic blood pressure, *FBG* fasting blood glucose, *PBG* postprandial blood glucose, *SBP* systolic blood pressure, *SOS* speed of sound, *BUA* broadband ultrasound attenuation, *QUI* quantitative ultrasound index

0.968]; PBG ≥ 15.0 mmol/L: 0.700 [0.520, 0.941]; HbA1C 6.5–7.5 %: 0.677 [0.523, 0.877] and HbA1C ≥ 7.5 %: 0.723 [0.538, 0.972]). Moreover, significant trend between osteopenia and SBP, FBG, PPG and HbA1C was observed in women. In contrast, no significant associations between osteopenia and DBP, TC, TG, HDL-C, LDL-C were found, and no significant trend relationship between osteopenia and DBP, TC, TG, HDL-C, LDL-C was found in postmenopausal Chinese women.

Discussion

In this study, we evaluated relationships between osteopenia and diabetes and cardiovascular risks in postmenopausal Chinese women. Decreasing prevalence of osteopenia was shown to be associated with rising SBP, FPG, PPG and HbA1C. However, no significant associations were found between osteopenia and DBP, TC, TG, HDL-C and LDL-C.

Researches on the relationship between blood pressures and BMD have generated controversial findings. In the present study, SBP and the prevalence of osteopenia have positive correlation which is difficult to explain. This finding was supported by Hanley et al. [7], who found a positive relation between hypertension and lumbar spine, femoral neck and trochanter BMD. Lidfeldt et al. [8] study also demonstrated that the wrist BMD was associated with systolic and diastolic blood pressure in postmenopausal women. However, one study reported higher blood pressure in elderly white women is associated with increased bone loss at the femoral neck [9]. Another study reported

Table 2 Relationships between osteopenia and selected cardiovascular risk factors

	Model 1		Model 2		Model 3	
	OR (95 % CI)	*P* value	OR (95 % CI)	*P* value	OR (95 % CI)	*P* value
History of CVD	1.005 (0.797, 1.268)	0.966	0.982 (0.770, 1.252)	0.881	0.991 (0.775, 1.266)	0.940
DBP						
<80 mmHg	Reference		Reference		Reference	
80–89 mmHg	0.877 (0.744, 1.034)	0.119	0.929 (0.781, 1.105)	0.406	0.966 (0.810, 1.151)	0.697
≥90 mmHg	0.788 (0.579, 1.071)	0.128	0.770 (0.558, 1.063)	0.112	0.820 (0.591, 1.137)	0.235
P value for trend	0.883 (0.784, 0.995)	0.041	0.901 (0.795, 1.021)	0.103	0.933 (0.821, 1.060)	0.287
SBP						
<120 mmHg	Reference		Reference		Reference	
120–139 mmHg	0.800 (0.682, 0.939)	0.006	0.837 (0.707, 0.991)	0.039	0.869 (0.732, 1.031)	0.107
≥140 mmHg	0.719 (0.593, 0.871)	**0.001**	0.726 (0.59, 0.888)	0.002	0.781 (0.636, 0.959)	**0.018**
P value for trend	0.845 (0.768, 0.929)	0.001	0.851 (0.770, 0.941)	0.002	0.883 (0.797, 0.978)	**0.017**
TC						
≤4.14 mmol/L	Reference		Reference		Reference	
4.15–5.18 mmol/L	0.984 (0.774, 1.250)	0.89	0.936 (0.731, 1.198)	0.709	1.067 (0.830, 1.371)	0.615
5.19–6.22 mmol/L	0.932 (0.736, 1.181)	0.560	0.971 (0.760, 1.124)	0.487	0.937 (0.731, 1.201)	0.610
>6.22 mmol/L	0.948 (0.725, 1.239)	0.696	0.887 (0.674, 1.168)	0.852	0.993 (0.750, 1.313)	0.959
P value for trend	0.975 (0.903, 1.053)	0.526	0.964 (0.890, 1.044)	0.370	0.969 (0.894, 1.050)	0.444
TG						
<1.70 mmol/L	Reference		Reference		Reference	
1.70–2.82 mmol/L	0.881 (0.752, 1.033)	0.118	0.887 (0.752, 1.047)	0.156	0.936 (0.791, 1.107)	0.439
≥2.83 mmol/L	0.786 (0.612, 1.009)	0.059	0.775 (0.596, 1.008)	0.058	0.800 (0.614, 1.043)	0.100
P value for trend	0.885 (0.795, 0.984)	0.024	0.883 (0.790, 0.987)	0.029	0.909 (0.812, 1.018)	0.100
HDL-c						
<1.03 mmol/L	0.846(0.661, 1.083)	0.184	0.794 (0.608, 1.035)	0.089	Reference	
1.03–1.54 mmol/L	0.913 (0.791, 1.054)	0.216	0.870 (0.746, 1.014)	0.075	0.851 (0.650, 1.116)	0.243
≥1.55 mmol/L	Reference		Reference		0.918 (0.784, 1.074)	0.286
P value for trend	1.155 (1.034, 1.291)	0.011	1.133 (1.009, 1.273)	0.035	1.086 (0.964, 1.224)	0.177
LDL-c						
<3.37 mmol/L	Reference		Reference		Reference	
3.37–4.13 mmol/L	0.95 (0.815, 1.107)	0.509	0.908 (0.773, 1.066)	0.237	0.919 (0.862, 1.080)	0.304
≥4.14 mmol/L	0.943 (0.771, 1.153)	0.569	0.937 (0.760, 1.155)	0.542	0.943 (0.764, 1.164)	0.585
P value for trend	0.966 (0.880, 1.061)	0.469	0.954 (0.866, 1.051)	0.341	0.959 (0.869, 1.058)	0.401

Model 1 included age for adjustment

Model 2 included the covariate in model 1 and also physical activity, smoking, alcohol consumption, age at menopause

Model 3 included the covariates in model 2 and also BMI for adjustment

no relationship between proximal femoral BMD and hypertension, which was found in postmenopausal non-Hispanic white, non-Hispanic black and Mexican–American women [10]. Studies data have yielded conflicting results, perhaps because of the limited data available, the technological diversity of the BMD devices, the different populations studied, the various age ranges and the variety of sites measured. Taken together, the potential mechanisms are complex. None of these authors could offer a satisfactory physiopathological explanation for positive findings. On the contrary, in other studies an inverse relation between hypertension and BMD was explained via abnormal calcium metabolism, secondary parathyroid hormone secretion or sodium intake [11–13].

Serum lipids and lipoproteins are also argued to be associated with BMD. Serum lipid levels have a prominent role in the pathogenesis of CVD. Some [14, 15] observational studies found that treatment of CVD with statins, lipid-lowering drugs, was associated with a significantly reduced fracture risk and increased BMD. Therefore, the question arises whether lipids are associated with the pathogenesis of low BMD. One study reported that BMD

Table 3 Relationships between low BMD and parameters relevant to diabetes

	Model 1		Model 2		Model 3	
	OR (95 % CI)	*P* value	OR (95 % CI)	*P* value	OR (95 % CI)	*P* value
Diagnosed T2DM	0.798 (0.677, 0.941)	0.007	0.772 (0.650, 0.916)	0.003	0.797 (0.669, 0.948)	**0.010**
FPG						
<6.1 mmol/L	Reference		Reference		Reference	
6.1–6.9 mmol/L	0.958 (0.749, 1.225)	0.739	0.876 (0.696, 1.103)	0.261	1.008 (0.786, 1.292)	0.951
7.0–7.9 mmol/L	0.659 (0.473, 0.918)	**0.014**	0.678 (0.491, 0.937)	0.018	0.709 (0.506, 0.994)	**0.046**
≥8.0 mmol/L	0.720 (0.541, 0.958)	**0.024**	0.792 (0.597, 1.051)	0.106	0.726 (0.544, 0.968)	**0.029**
P value for trend	0.883 (0.812, 0.959)	0.003	0.899 (0.829, 0.975)	0.010	0.895 (0.822, 0.973)	**0.010**
PPG						
<11.1 mmol/L	Reference		Reference		Reference	
11.1–12.9 mmol/L	0.924 (0.684, 1.249)	0.609	0.836 (0.630, 1.109)	0.214	0.956 (0.707, 1.293)	0.770
13.0–14.9 mmol/L	0.767 (0.552, 1.065)	0.113	0.753 (0.550, 1.033)	0.078	0806 (0.577, 1.127)	0.208
≥15.0 mmol/L	0.690 (0.513, 0.926)	**0.014**	0.729 (0.544, 0.976)	0.034	0.700 (0.520, 0.941)	**0.018**
P value for trend	0.884 (0.811, 0.963)	0.005	0.888 (0.817, 0.966)	0.005	0.894 (0.820, 0.974)	**0.011**
HbA_{1c}, %						
<6.50	Reference		Reference		Reference	
6.50–7.49	0.638 (0.495, 0.824)	**0.001**	0.658 (0.521, 0.831)	<0.001	0.677 (0.523, 0.877)	**0.003**
≥7.50	0.715 (0.533, 0.960)	**0.025**	0.810 (0.610, 1.074)	0.143	0.723 (0.538, 0.972)	**0.032**
P value for trend	0.795 (0.697, 0.906)	0.001	0.836 (0.738, 0.946)	0.005	0.809 (0.709, 0.923)	**0.002**

Model 1 included age at enrollment for adjustment

Model 2 included the covariate in model 1 and also physical activity, smoking, alcohol consumption, age at menopause

Model 3 included the covariates in model 2 and also BMI for adjustment

was inversely correlated with low HDL-C and elevated TG levels in South Korean men [16]. However, an absent [17, 18] or even a positive [19] relationship has also been reported. In the present study, no significant associations were found to be related to low BMD.

Regarding the relationships between low BMD and parameters relevant to type 2 diabetes mellitus (T2DM), despite a high incidence of fragility fracture in T2DM patients, data on bone change in T2DM were conflicting, ranging from decrease, no change or increase in BMD [20–22]. In the present study, decreasing prevalence of osteopenia was shown to be associated with rising FPG, PPG and HbA1C. The result suggests that bone change in diabetic women may be more complicated and need alternative marker to predict the fracture risk.

There are several limitations in the present study. First, the causal relationship between SBP, FPG, PPG, HbA1C and osteopenia cannot be established based on the nature of our cross-sectional study. Second, we used calcaneal quantitative ultrasound (QUS) as a measurement rather than dual X-ray absorptiometry (DXA) to assess BMD, although meta-analysis of prospective studies shows that QUS using validated devices predicts risk of different types of fracture with similar performance across different devices and in elderly men and women. Finally, we did not exclude subjects who underwent pharmaceutical therapies for CVD, hypertension and T2DM, which might affect bone metabolism. Further studies are needed to fully ascertain the mechanisms underlying the association between osteopenia and diabetes.

In conclusion, the present study showed a relationship between SBP, FBG, PPG, HbA1C and osteopenia in postmenopausal Chinese women, while no significant relationship was observed between dyslipidemia, DBP and osteopenia, even after controlling for multiple confounding factors. Bone change in diabetic women may be more complicated and need alternative marker to predict the osteopenia.

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Compliance with ethical standards

Conflict of interest None.

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