



Lipid profiles as potential mediators linking body mass index to osteoporosis among Chinese adults: the Henan Rural Cohort Study

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Abstract

Summary This study is to examine the relationship between body mass index (BMI) and osteoporosis in rural areas of China, and then explore whether this association was mediated by lipid profiles. Results showed that with the increasing of BMI, the risk of osteoporosis was reduced, and lipid profiles mediate this association.

Introduction To examine the relationship between BMI and osteoporosis, and explore whether this association was mediated by lipid profiles.

Methods A total of 8272 participants (18–79 years) were enrolled from the Henan Rural Cohort Study. The bone mineral density of the calcaneus was measured using an ultrasonic bone density apparatus. Logistic regression and restricted cubic splines were used to evaluate the odds ratio (OR) and 95% confidence intervals (95% CI). Mediation analysis using bootstrap was performed to examine the contribution of lipid profiles to BMI-related osteoporosis.

Results The crude and age-standardized prevalence of osteoporosis were 15.93% and 11.77%, respectively. The mean BMIs were 24.12 kg/m² for participants with osteoporosis and 25.06 kg/m² for non-osteoporosis participants ($P < 0.001$). After adjusting for potential confounders, subjects with obesity had a lower OR of osteoporosis (0.493 [95% CI: 0.405–0.600], $P_{\text{trend}} < 0.001$) compared with normal-weight individuals. Mediation analysis showed that lipid profile partly mediated the relationship between BMI and osteoporosis with indirect effect OR (95% CI) of 0.985 (0.978–0.992), and the proportion explained of BMI was 15.48% for lipid profile.

D.Y. Wu and D. Qiao contributed equally to this work.

What is already known on this subject?

Previous studies have shown that obesity was associated with osteoporosis, but studies were conducted mostly concentrated on the medical examination crowd. In addition, studies focusing on rural adults are still limited. More importantly, studies exploring whether lipid profile mediates body mass index-related osteoporosis have not been reported yet.

What does this study add?

The results of this study indicated that body mass index was significantly associated with osteoporosis in a Chinese rural population aged 18–79 years. In addition, the present study was the first one examined whether blood lipids mediate BMI-related osteoporosis, and the results indicated that lipid profile partly mediated the relationship between body mass index and osteoporosis. The findings provide evidence to the clinical physicians and public health researchers for future osteoporosis prevention among a high-risk population with low body mass index.

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Conclusion With the increasing of BMI, the risk of osteoporosis was reduced in the Chinese adult population, and lipid profiles may be a potential mediator linking reduced risk of osteoporosis. Elucidating the underlying mechanisms will facilitate developing feasible preventive and therapeutic measures for osteoporosis.

Chinese clinical trial register: ChiCTR-OOC-15006699.

Keywords Body mass index · Bone mineral density · Mediation analysis · Obesity · Osteoporosis

Introduction

Osteoporosis has become an important public health problem because of the relative aging of the world population and longer life expectancies. According to recent prevalence estimates from the National Health and Nutrition Examination Survey (NHANES), the prevalence of osteoporosis ranged from 6 to 11%, while the prevalence of low bone mass ranged from 28 to 45% of US adults aged ≥ 50 years in 2013–2014 [1]. A survey estimated that about 69.44 million Chinese adults aged ≥ 50 years had osteoporosis, and about 210 million had low bone density in 2006 [2]. Osteoporosis is an important contributor to the public health burden, because it increases the risk of fractures, which imposes a substantial burden of disability, costs, and mortality on postmenopausal women and older men [3]. Thus, to prevent this public health problem in China, finding out the determinants of osteoporosis is urgently needed.

There have been several studies showing that obesity was associated with osteoporosis [4–7]. Previous studies demonstrated that body mass index (BMI), fat mass, and lean mass are beneficial for bone mineral density (BMD) in both males and postmenopausal females [8, 9]. A cross-sectional study conducted in Brooklyn including only women aged 50 years or older reported that there was a race-dependent effect of BMI on BMD. While a slight but significant decrease in BMD was present in African American women, the BMD increased with each unit increase in BMI in Caucasian women [10]. A hospital-based study conducted in Changsha, China, including 269 postmenopausal women indicated that BMD of subjects with obesity was significantly higher than that in the control group [11]. Studies conducted in China are mostly concentrated on individuals coming in for a medical examination, but reports from the rural areas are scarce. More importantly, what factors mediate this relation remains so far poorly studied. The objective of this study was to examine the relationship between BMI and osteoporosis in a Chinese adult population. In addition, we hypothesized that this association was mediated to some degree by blood lipids because an array of evidence support associations of lipid profile with both BMI [12, 13] and osteoporosis [14–16].

Methods

Study subjects

The study subjects were derived from the Henan Rural Cohort Study performed in the rural areas in Henan province from July 2015 to September 2017, which has been registered before the onset of patient enrollment in the Chinese Clinical Trial Register (Registration number: ChiCTR-OOC-15006699). A multistage, stratified cluster sampling method was used to select samples. Among 39,259 participants aged 18–79 years, only the 8475 subjects that completed the BMD measurement were included. Subjects were also excluded if they did not have BMI data ($n = 5$) and BMI < 18.5 kg/m² ($n = 198$). Finally, 8272 eligible subjects were included for the present analysis. This study was approved by the Zhengzhou University Life Science Ethics Committee, and all participants provided written informed consent.

Assessment of bone mineral density

The bone mineral density of the calcaneus was measured three times using an ultrasonic bone density apparatus (Hologic Sahara, USA), a practical and reliable tool for detecting osteoporosis [17]. The BMD T-score was calculated from the manufacturer-provided reference data, which was derived from a database of young healthy Chinese individuals, and the average of the three readings was taken for analysis. The diagnosis of osteoporosis/osteopenia was done according to T-score values: normal, T-score ≥ -1.0 ; osteopenia, $-2.5 < \text{T-score} < -1.0$; osteoporosis, T-score ≤ -2.5 [18].

Definition of mediators

After overnight fasting, venous blood samples were drawn from the participants, serum was separated by centrifugation at 3000 rpm for 10 min at room temperature, and a Roche Cobas C501 automatic biochemical analyzer was used to determine total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) in the samples.

Assessment of potential covariates

The information on demographic, socioeconomic, and lifestyle factors (e.g., smoking, alcohol drinking, dietary habits, physical activity levels, and medical history) was collected through face-to-face interview by trained research staff using a standardized questionnaire. Education level was divided into elementary school or below, junior high school, and high school or above. According to the smoking index of the World Health Organization (WHO) [19], smoking status was grouped into never smoking, light smoking, moderate smoking, and heavy smoking. In accordance with the daily alcohol intake of WHO and the dietary guidelines for Chinese residents [19, 20], drinking was divided into four categories: never drinking, light drinking, moderate drinking, and heavy drinking. Based on the International Physical Activity Questionnaire (IPAQ 2001), physical activity was grouped into low, moderate, and high level [21].

While the subjects wore light clothing and without shoes, hats, and coats, their heights and weights were measured twice with the metric scale and the vertical weight scale following a standardized protocol [22], and the readings were taken to the nearest 0.1 cm and 0.1 kg, respectively. The body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m). According to the criteria recommended by WGOC [23], participants were categorized into three BMI groups: normal weight, BMI < 24.0 kg/m²; overweight, 24.0 kg/m² ≤ BMI < 28.0 kg/m²; and general obesity, BMI ≥ 28.0 kg/m². According to the American Heart Association's standardized protocol [24], blood pressure (BP) was measured three times for each participant with an electronic sphygmomanometer (HEM-770AFuzzy, Omron, Japan), and the average of the three readings was taken for the analysis.

Statistical analysis

Participants were divided into two categories: non-osteoporosis, T-score > -2.5, and osteoporosis, T-score ≤ -2.5. Characteristics of the participants were described as numbers (percentages) for categorical variables, and mean ± standard deviation (SD) for continuous variables. Differences in the clinical characteristics of patients were determined with the chi-square test for categorical variables and *t* test for continuous variables. The age-standardized prevalence of osteoporosis was calculated according to data from the sixth census in China. Restricted cubic splines with knots at the 20th, 40th, 60th, and 80th percentiles of BMI levels were performed to explore the relationship between BMI and BMD. In addition, the linear correlation and linear regression model were also conducted to assess BMI and BMD among different age and gender groups.

Logistic regression models were applied to evaluate the association of BMI group with osteoporosis with

adjustment for potential confounders. In addition, non-linear trends of the relationship between BMI and risk for osteoporosis was tested by restricted cubic splines logistic regression using four knots at the 20th, 40th, 60th, and 80th percentiles of BMI levels, with 20 kg/m² (approximating the first knot) as the reference group.

To determine potential mediators of the association between BMI and osteoporosis, principal component analysis of blood lipid indices (TC, TG, HDL-C, and LDL-C) was performed to create continuous variables. An eigenvalue ≥ 1 was used as a cutoff for factor retention. Then mediation analysis using bootstrap was performed to address whether BMI-related decreased risk of osteoporosis was explained by lipid profile (TC, TG, HDL-C, LDL-C). The direct and indirect effects were estimated at the mean level of mediators, and the “proportion explained” was calculated using the formula $(OR_{TE} - OR_{NDE}) / (OR_{TE} - 1)$ [25], where OR_{TE} is the total effect odds ratio and OR_{NDE} is the direct effect odds ratio. Statistical difference found in indirect effect but not in direct effect was called complete mediation. Partial mediation exists when indirect and direct effects are significant.

All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. SAS 9.1 software package (SAS Institute, USA) and SPSS 21.0 were used to perform statistical analyses.

Results

Demographic characteristics of the participants

The general characteristics of the population are shown in Table 1. Overall, 1318 participants (367 men and 951 women) were diagnosed with osteoporosis, and the mean age was 58.88 ± 10.73 years. For participants with osteoporosis, the mean BMD was 0.31 g/cm², and for non-osteoporosis this was 0.47 g/cm² ($P < 0.001$). The mean BMI for participants with osteoporosis was lower than non-osteoporosis ($P < 0.001$); corresponding values were 24.12 kg/m² and 25.06 kg/m², respectively. Among non-osteoporosis participants, married/cohabiting, smoking, drinking, higher fasting blood glucose, and higher total cholesterol were more common. In contrast, among osteoporosis participants, older age, female gender, lower education level, lower average monthly individual income, high physical activity, higher high-density lipoprotein cholesterol, and higher low-density lipoprotein cholesterol were more prevalent.

Prevalence of osteoporosis per BMI group

Overall, the crude prevalence of osteoporosis was 15.93% and the age-standardized prevalence of osteoporosis was 11.77%. The mean BMDs were 0.44 ± 0.11 g/cm² for normal weight,

Table 1 Demographic and clinical characteristics of study participants

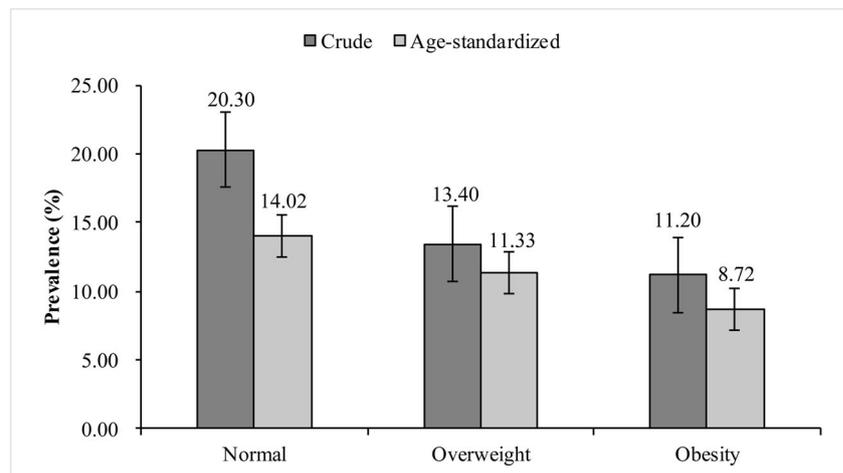
Characteristics	Non-osteoporosis (<i>n</i> = 6954)	Osteoporosis (<i>n</i> = 1318)	<i>P</i> value
Age (mean ± SD)	53.93 ± 11.36	58.88 ± 10.73	< 0.001
Men, <i>n</i> (%)	2959 (42.60)	367 (27.8)	< 0.001
Education level, <i>n</i> (%)			< 0.001
Elementary school or below	2792 (40.10)	757 (57.40)	
Junior high school	2787 (40.10)	411 (31.20)	
High school or above	1375 (19.80)	150 (11.40)	
Average monthly individual income, <i>n</i> (%)			0.036
< 500 RMB	2333 (33.50)	487 (36.90)	
500–1000 RMB	2110 (30.30)	395 (30.00)	
≥ 1000 RMB	2511 (36.10)	436 (33.10)	
Marital status, <i>n</i> (%)			< 0.001
Married/cohabitating	6417 (92.30)	1156 (87.70)	
Unmarried/divorced/widowed	573 (7.70)	162 (12.30)	
Smoking, <i>n</i> (%)			< 0.001
Never	4840 (72.00)	1024 (80.31)	
Light	382 (5.68)	40 (3.14)	
Moderate/heavy	1500 (22.31)	211 (16.55)	
Drinking, <i>n</i> (%)			< 0.001
Never	5104 (75.93)	1052 (82.51)	
Light	974 (14.49)	132 (10.35)	
Moderate/heavy	644 (9.58)	91 (7.14)	
Physical activity, <i>n</i> (%)			< 0.001
Low	2214 (31.80)	358 (27.20)	
Moderate	2467 (35.50)	450 (34.10)	
High	2273 (32.70)	510 (38.70)	
Dietary habits (g/week), (mean ± SD)			
Meat and poultry	45.81 ± 43.95	37.74 ± 41.74	< 0.001
Fishery products	4.24 ± 5.44	3.42 ± 4.84	< 0.001
Vegetables and fruits	509.65 ± 265.72	482.23 ± 244.41	0.001
Soy products	29.51 ± 34.97	24.48 ± 32.53	< 0.001
SBP (mmHg), (mean ± SD)	124.84 ± 19.55	126.21 ± 20.19	0.020
DBP (mmHg), (mean ± SD)	77.99 ± 11.53	76.49 ± 11.63	< 0.001
GLU (mmol/L), (mean ± SD)	5.48 ± 1.45	5.35 ± 1.41	0.003
TC (mmol/L), (mean ± SD)	4.82 ± 0.98	4.82 ± 0.96	0.991
TG (mmol/L), (mean ± SD)	1.71 ± 1.13	1.53 ± 0.94	< 0.001
HDL-C (mmol/L), (mean ± SD)	1.34 ± 0.33	1.44 ± 0.36	< 0.001
LDL-C (mmol/L), (mean ± SD)	2.92 ± 0.82	3.05 ± 0.86	< 0.001
BMI (kg/m ²), (mean ± SD)	25.06 ± 3.34	24.12 ± 3.31	< 0.001
BMD (g/cm ²), (mean ± SD)	0.47 ± 0.10	0.31 ± 0.08	< 0.001
T-score, (mean ± SD)	− 0.92 ± 1.07	− 2.94 ± 0.37	< 0.001

SD standard deviation, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *GLU* fasting blood glucose, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *BMI* body mass index, *BMD* bone mineral density

0.46 ± 0.11 g/cm² for overweight, and 0.48 ± 0.10 g/cm² for the obesity group. Per respective BMI group, the crude prevalence of osteoporosis was 20.30%, 13.40%, and 11.20%. There was a decreased trend of osteoporosis prevalence

considering the normal, vs. overweight, vs. obesity groups ($P < 0.001$). Per respective BMI group, the age-standardized prevalence of osteoporosis was 14.02%, 11.33%, and 8.72% (Fig. 1). What is more, prevalence rates of osteoporosis in the

Fig. 1 The crude and age-standardized prevalence of osteoporosis per BMI group. Black bars indicate 95% confidence interval



different age groups of the rural population in China are shown in the Online Resource (Supplemental Table 1). The prevalence was increased with the age groups ($Z = 14.01$, $P_{\text{trend}} < 0.0001$), and women had higher prevalence than men did after the age group of 40–49 ($P < 0.05$).

In spline regression models, bone mineral density levels increased with increasing BMI (Fig. 2). In addition, the linear correlation and linear regression of BMI and BMD showed that a positive correlation existed between BMI and BMD among different age and gender groups (Online Resource Supplemental Table 2).

The relationship between general obesity and osteoporosis

The results of the logistic regression analysis of the association between general obesity and osteoporosis are shown in Table 2. When compared with the normal group, the OR (95% CI) of osteoporosis for general obesity was 0.495 (0.411–

0.596) ($P_{\text{trend}} < 0.001$) in the univariate model, and after adjusting for age and gender, the corresponding effect value increased to 0.502 (0.415–0.607) ($P_{\text{trend}} < 0.001$) (model 2). Further additional adjustment for education level, marital status, smoking, drinking, physical activity, and dietary habits (model 3) did not substantially change the association (OR, 0.493 [95% CI: 0.405–0.600], $P_{\text{trend}} < 0.001$). The fully adjusted ORs for each 1 SD increment in BMI were 0.796 (95% CI: 0.756–0.838) for osteoporosis. Besides, similar results were shown in the men and women aged over 50 (Online Resource Supplemental Table 3). In addition, in all three applied models, the restricted cubic splines demonstrated a non-linear dose-response relationship between BMI and the risk of osteoporosis ($P < 0.05$) (Fig. 3).

Mediators of the effect of BMI on osteoporosis

Principal component analysis of the blood lipids index (TC, TG, HDL-C, and LDL-C) resulted in the creation of two

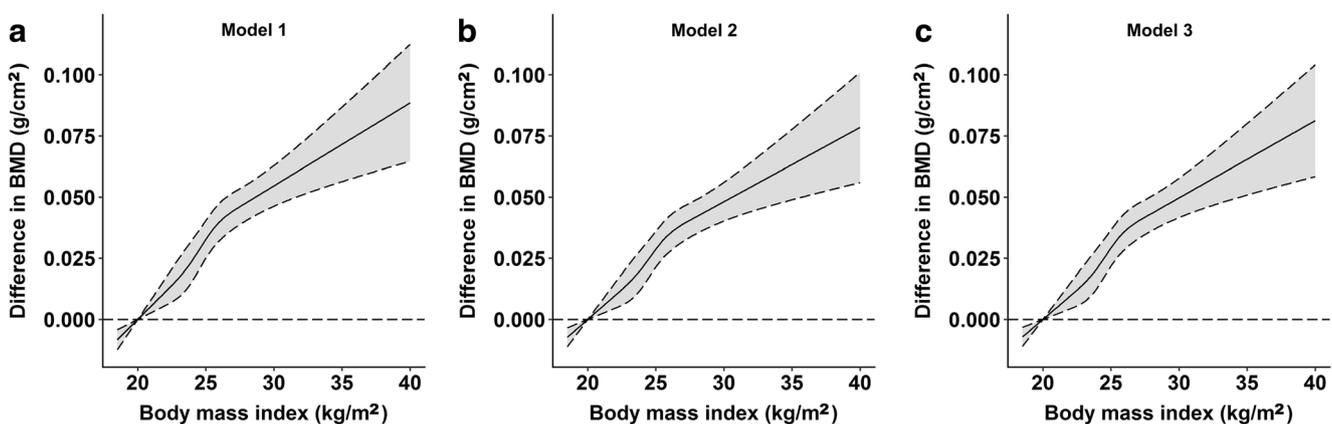


Fig. 2 Differences (95% confidence intervals) for bone mineral density levels plotted against BMI. The body mass index was modeled as restricted cubic splines with nodes at the 20th, 40th, 60th, and 80th percentiles. **a** Model 1: unadjusted. **b** Model 2: adjusted covariates for

age and gender. **c** Model 3: additionally adjusted for education level, marital status, smoking, drinking, physical activity, and dietary habits (meat and poultry, fishery products, vegetables and fruits, and soy products).

Table 2 Odds ratios (95% CI) for the risk of osteoporosis per BMI group

	Normal weight	Overweight	Obese	P_{trend}	BMI Per 1 SD increment
Model 1	1.00	0.604 (0.531–0.687)	0.495 (0.411–0.596)	< 0.001	0.751 (0.706–0.799)
Model 2	1.00	0.599 (0.525–0.683)	0.502 (0.415–0.607)	< 0.001	0.755 (0.708–0.804)
Model 3	1.00	0.590 (0.515–0.675)	0.493 (0.405–0.600)	< 0.001	0.796 (0.756–0.838)

Model 1: unadjusted. Model 2: adjusted covariates for age and gender. Model 3: additionally adjusted for education level, marital status, smoking, drinking, physical activity, and dietary habits (meat and poultry, fishery products, vegetables and fruits, and soy products)

continuous variables (principal component I and principal component II*), and accumulative contribution was 84.42% of total variance. Therefore, in mediation analysis, we performed that two principal components (PC) mediated this association of BMI-osteoporosis. The results of mediation analysis show that principal component II partly mediated the relationship between BMI and osteoporosis with an indirect-effect OR (95% CI) of 0.985 (0.978–0.992) (Fig. 4). The proportion explained of BMI was 15.48% for lipid profile.

*Principal component I (PC I) = $0.971 \times \text{TC} + 0.134 \times \text{TG} + 0.301 \times \text{HDL-C} + 0.932 \times \text{LDL-C}$

Principal component II (PC II) = $0.135 \times \text{TC} + 0.884 \times \text{TG} - 0.810 \times \text{HDL-C} - 0.006 \times \text{LDL-C}$

Discussion

To the best of our knowledge, the study is the first that reported the relationship including mediator effects between obesity

and osteoporosis in a Chinese rural population. The major findings are as follows: (i) the mean BMI for participants with osteoporosis was lower than that for non-osteoporosis participants; (ii) a decreasing trend of osteoporosis prevalence was observed from normal to the obesity group, but in spline regression models the BMD levels increased with increasing BMI; (iii) subjects with obesity showed a lower risk of osteoporosis compared with normal-weight adults after adjusting for various conventional osteoporosis risk factors; and (iv) the lipid profile partly mediated the relationship between BMI and osteoporosis.

The strong inverse association between BMI and osteoporosis was observed in our study contributing to the profound research on the topic. The fact that weight led to decreases in hip BMD significantly but had less effect on the spine was revealed in a systematic review and meta-analysis including 32 randomized controlled trials in 2016 [26]. Weight loss response following caloric restriction led to a decrease in hip and lumbar spine bone density, especially when the weight loss period was more than 1 year, whereas an exercise-induced weight loss did not. A study involving a middle-aged non-institutionalized population in the USA reported that the increasing BMI could protect the bone mineral density

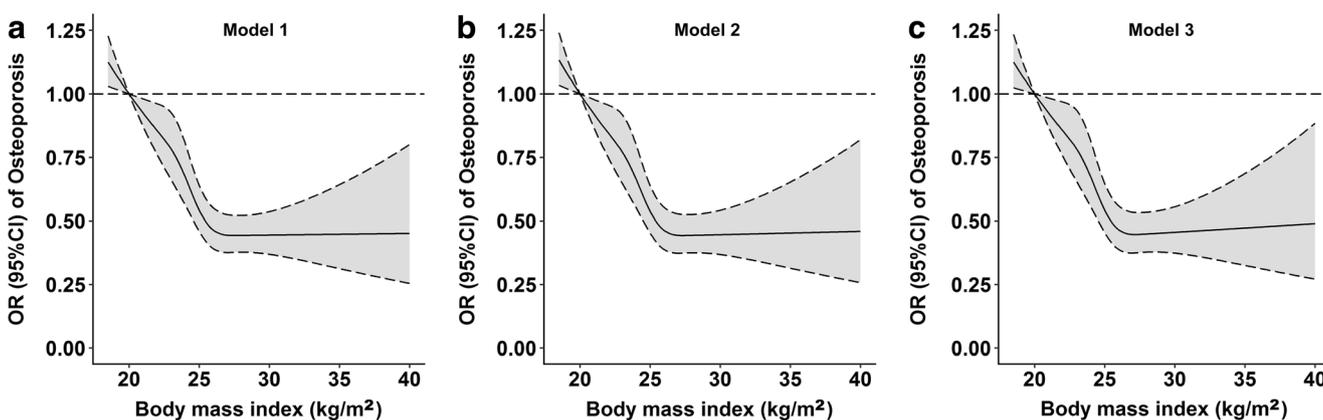


Fig. 3 OR (solid lines) and 95% CI (dashed lines) for the risk of osteoporosis along with the changes of BMI from the restricted cubic splines regression model. **a** Model 1: unadjusted. **b** Model 2: adjusted covariates for age and gender. **c** Model 3: additionally adjusted for

education level, marital status, smoking, drinking, physical activity, and dietary habits (meat and poultry, fishery products, vegetables and fruits, and soy products)

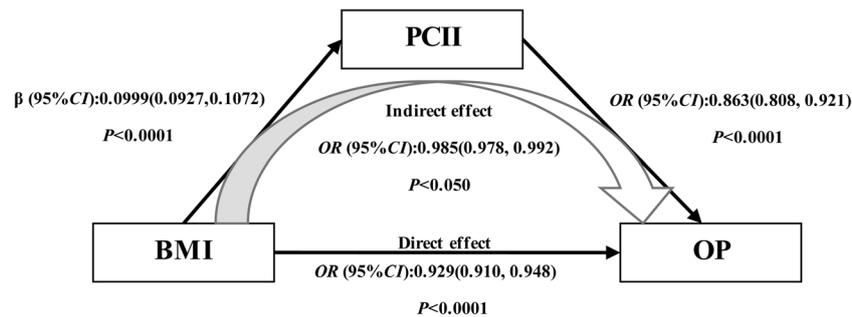


Fig. 4 Mediation analysis to determine the relationship between BMI and osteoporosis through lipid profiles. Abbreviations: BMI, body mass index; OP, osteoporosis; PCII, principal component II = $0.135 \cdot TC + 0.884 \cdot TG - 0.810 \cdot HDL-C - 0.006 \cdot LDL-C$. Odds ratio (OR; 95% CI; P

value) of total effect was 0.914 (0.896–0.932; $P < 0.0001$). Adjusted for age, gender, education level, marital status, smoking, drinking, physical activity, and dietary habits (meat and poultry, fishery products, vegetables and fruits, and soy products).

from decreasing, especially for the individuals with osteoporosis in which a 10-unit increase in BMI would help the BMD level to become normal [7]. A prospective cohort study in Eastern Finland including only postmenopausal women found that women with a baseline BMI of 20 kg/m² would become osteopenic after menopause by 2–4 years, while a BMI of 30 kg/m² delayed the occurrence of osteopenia by 5–9 years [27]. Although the previous studies recruited a relatively large number of subjects, they did not specifically include a rural population. In this study, we analyzed the largest number of subjects of both sexes with a wide age range in the rural areas of China, which is a strength of our study.

Multiple lines of evidence support associations of altered lipid profiles with BMI. In the Japanese population, percent changes in BMI were found to be an independent predictor of inverse changes in lipid parameters in both genders [12]. A cross-sectional study conducted in the Physical Examination Center of the Chinese PLA General Hospital using data from a national health survey showed that BMI was positively associated with LDL-C, TC, and TG, and inversely associated with HDL-C [13]. What is more, associations between lipid parameters and BMD were also examined previously. In a Taiwanese elderly population, a positive association was identified between HDL-C and BMD in women, while this association in men was opposite [14]. Two studies conducted in Italy and England showed that total body and hip BMD were significantly related to serum lipids in both women and men. The relationship was negative for HDL-C, and positive for total cholesterol, triglycerides, and LDL cholesterol [15, 16]. In the present study, we found that lipid profile might play a mediated role on the effect that BMI decreased the prevalence of osteoporosis. Besides, principal component analysis of blood lipid indices (TC, TG, HDL-C, and LDL-C) created two continuous variables and the accumulative contribution was 84.42% of total variance. In the present analysis, we reported that 15.48% of excess relative risk of osteoporosis was mediated through the lipid profile in relation to BMI.

To interpret the complex relationship between adipose tissue and bone, several potential mechanisms have been

proposed. It cannot be ignored that the bones of a subject with greater BMI are subjected to greater stress by gravity, and this can potentially explain the correlation between BMI and BMD. However, it is possible to hypnotize other causes, such as an interference of fat metabolism with osteogenesis. In spite of this, it should be specified that the correlation between the metabolism of the peripheral blood fat and subcutaneous fat and the bone metabolism is mediated by the metabolism of the bone marrow fat [28, 29]. Adipocytes and osteoblasts originate from a common pluripotential mesenchymal stem cell, which has an equal tendency for differentiation into adipocytes or osteoblasts under the influence of several cell-derived transcription factors [30]. Some people hold that perturbation in HDL metabolic pathways favors adipoblastic and restrain osteoblastic differentiation through, among others, the modification of specific bone-related chemokines and signaling cascades [31]. In fact, adipose tissue secretes various inflammatory cytokines which are thought to contribute to the differentiation and function of osteoblasts, such as interleukin (IL)-6, resistin, leptin, adiponectin, and tumor necrosis factor α (TNF α) [32–34], while reduced HDL levels have been associated with the development of an inflammatory microenvironment [35, 36]. Furthermore, estrogens synthesized by aromatases play a pivotal role in protecting against osteoporosis by reducing bone resorption, stimulating bone formation, and the maintenance of skeletal homeostasis. Fat tissue is known to be one of the major sources of aromatase [37, 38].

The present study has several important strengths. We examined the relationship between BMI and osteoporosis with a relatively large sample size within the rural population in China, which included both men and women, as well as young and elderly people. The standardized survey tools, the training and field implementation, and the adjustment for a wide range of potential confounders guarantee the reliability of the analysis. In addition, mediation analysis was performed to address whether the relation between BMI and reduced risk of osteoporosis was explained by lipid profile, and we calculated the proportion explained based on the pooled natural direct and indirect effects. Furthermore, the relevant mediators were

determined by principal component analysis. Nevertheless, several limitations also warrant consideration. First, these findings were derived from a cross-sectional study; therefore, causal and temporal associations could not be inferred. Secondly, the BMD of the calcaneus was measured using an ultrasonic bone density apparatus (Hologic Sahara, USA); albeit dual-energy X-ray absorptiometry is considered to be the gold standard for measuring bone mineral density and osteoporosis diagnosis, its application in large-scale population studies is very limited. A study indicated that there was no significant difference between the QUS and X-ray densitometric BMD methods in separating normal from osteoporotic subjects when using ROC analysis [39]. In addition, the same method has been applied in an elderly Chinese population [40] and some large cohort studies [41, 42]. Although the accuracy of ultrasonic measurement is limited, it can reflect the BMD of the study subjects to some extent, which is acceptable in the epidemiological investigation of large samples and can be used for the screening of osteoporosis. In addition, mediation analysis showed that lipid profile explains in part the relation between BMI and BMD, which may be due to that only lipid profile was included in the analysis, and other possible influencing factors (for instance, perhaps insulin levels, osteocalcin, and glycemia may influence lipid profile and bone) were not included in the analysis. More research involving other factors is needed. Finally, the subjects were only from one province accounting for 10% of China's rural population, which might not be a representative sample of the total Chinese rural population. Thus, to verify these findings, further prospective and multicultural studies are needed. Although the present study has these limitations, to some extent, the results based on a relatively large rural epidemiological study could represent the relationship between BMI and osteoporosis in Chinese rural areas.

With the increasing of BMI, the risk of osteoporosis was reduced in the Chinese rural population; lipid profiles may be a potential mediator linking reduced risk of osteoporosis. The findings provide an important basis for further research into the lipid parameters that are related to BMI, and which have the capacity to decrease the risk of developing osteoporosis, as they may represent new targets to develop preventive and therapeutic approaches against osteoporosis.

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Availability of data and material All data generated or analyzed during this study are included in this published article.

Authors' contribution CJW and JP conceived and designed the experiments. DQ, DYW, XZ, HQZ, ZCL, and YW performed and conducted the experiments. DQ, XZ, HQZ, ZCL, and YW analyzed the data and took responsibility for the integrity and accuracy of the information. DQ,

DYW, XZ, and HQZ contributed to the reagents/materials/analysis tools. DQ and DYW drafted and revised the manuscript. All authors have approved the final manuscript.

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Compliance with ethical standards

Conflicts of interest None.

Ethics approval Ethics approval was obtained from the “Zhengzhou University Life Science Ethics Committee,” and written informed consent was obtained for all participants. Ethic approval code: [2015] MEC (S128).

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