CLINICAL INVESTIGATION

Osteoporosis risk-assessment related lifestyle and metabolic factors: A population-based study

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Abstract

Background: Several studies have investigated the risk factors for osteoporosis in China, but little is known about the situation of osteoporosis in Southern China in recent years. Our present study investigates the osteoporosis risk factors of total population, male population and female population in Southern Chinese community-based population, aiming to suggest more effects for prevention and control of osteoporosis.

Materials: A multistage stratified random cluster sampling design was used in this cross-sectional study conducted in 2015. Osteoporosis was defined as T scores ≤ -2.5 at root bone. Unconditional and multivariate logistic regression analysis was used to calculate Odds Ratios (ORs) and 95% Confidence Intervals (CIs). Propensity Score (PS) matching analysis and Receiver Operating Characteristic (ROC) curve were used to control potential confounding and evaluate the predictive value of prediction model, respectively.

Results: The estimated prevalence of osteoporosis in Southern China of Guangzhou was 16.69%. Osteoporosis was positively associated with age, education level, vitamin D intake, physical activity, weight, neck circumference, waistline and total cholesterol level in total population. Increased weight level was association with low risk of osteoporosis. Besides, erectile dysfunction subjects with low bone mineral density in male population and menopause was independent risk factor for development of osteoporosis in female population. What's more, occasional and moderate drinking was protective factor for osteoporosis only in female population. Our study suggests that the roles of fat distribution but not only for fat quantity should be taken seriously to explore the association with osteoporosis.

Conclusion: We observed a high prevalence of osteoporosis among the Southern China in Guangzhou City. Meanwhile, our study lends support that some related lifestyle and metabolic factors may be the association factors for the development of osteoporosis. Government and health department should take measures to improve people's awareness of osteoporosis and reduce the prevalence of osteoporosis in Southern China. Our results will provide latest scientific evidence for health policy formulating.

Keywords: osteoporosis • risk factors • erectile dysfunction • drinking • menopause

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Abbreviations

ORs: Odds Ratios; CIs: Confidence Intervals; PS: Propensity Score; ROC: Receiver Operating Characteristic Curve; BMD: Bone Mineral Density; SDs: Standard Deviations; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TC: Total Cholesterol; TG: Triglycerides; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; BMI: Body Mass Index; NC: Neck Circumference; WC: Waist Circumference; MET: One Metabolic Equivalent; AUC: Area Under The Curve

Introduction

Osteoporosis is an increasingly common chronic disease that has a great effect not only in regard to clinical effects, but also in regard to economic burden worldwide. According to the World Health Organization (WHO) statistics, osteoporosis have become an important public health problem worldwide, one in three women and one in five men over 50 years of age will have an osteoporotic fracture in their lifetime [1]. Osteoporotic fractures cause enormous healthcare costs and reduce quality of life. In addition, osteoporotic are associated with increased mortality, functional decline, loss of quality of life, and a need for institutionalization in older subjects [2-4]. In developed countries, for example, the prevalence of osteoporosis in elderly was 13%-18% [5], and the mean prevalence rate of osteoporosis in China is about 15.7% among older adults [6-8], and it is considered to be increasing gradually with the increasing age worldwide [9]. China is a great developing and unbalanced developing country. As a result, Chinese government must change the strategy of healthy resource according to different crowd characteristics, regions, lifestyles and economic status to ensure the medical care for residents for Chinese. Guangzhou is one of the most representative cities for Southern China. Fast and high quality development economic strongly change the lifestyle and health care security, but the prevalence of several chronic diseases in this areas are still high. There is no doubt that the high prevalence and low awareness of osteoporosis will aggravate the burden on the Chinese medical system.

Osteoporosis, as one of the most common systemic skeletal disorder, is characterized by microarchitectural changes and low bone mass that increase the risk of bone fracture [10]. Fracture risk depends on bone strength, which is determined by bone quality and Bone Mineral Density (BMD) [11-14]. Osteoporosis and the associated risk factors have received much attention with the aging of the world population in the past 10 years [14-16]. Not only age is one of the main determinants risk of osteoporosis, the environmental factors, such as low body weight, low calcium and vitamin D intake, excessive tobacco use, alcohol consumption, and a sedentary lifestyle, as well as postmenopausal changes in women had been identified as the influencing factors of developing osteoporosis. But as the development of the living standards, the influencing factors changed. However, there are limited data concentrated on the status of osteoporosis and related disease surveillance till recently. Our present study was to investigate the prevalence and associated characteristics of osteoporosis in Guangzhou, Southern China. We aimed to suggest more efforts for the prevention and control the development of osteoporosis in Southern China Strengthen grassroots health care services system and conduct regular disease surveillance will achieve a remarkable medical economics in preventing and treating chronic diseases. Because of the different prevalence of osteoporosis in male and female population, we explored the risk factors for osteoporosis in total population, male population and female population. With the present study, we performed a cross-sectional study in two communities (rural/urban) by stratified cluster sampling. Guangzhou is located in the most Southern of China, the population living in the sea with lower height. People in there have different habits of living, with more seafood, lower salt diet and more sugar eating than other parts of China [17]. Compared with past, the presence people own more knowledge about health and trend to be more health [18]. We explore the influencing factors on osteoporosis and its change according to lifestyle and metabolic factors, perhaps.

Materials and Methods

Population

The subjects of this study were selected from people surveyed in the epidemiological investigation of thyroid nodules in a Chinese community-based population. In this project, we performed a cross-sectional study in two communities (rural/urban) by stratified cluster sampling in Guangzhou city, located in the South of China from March to July, 2015. **Inclusion criteria:** 1) 18-79 years old; 2) The Han ethnic of Chinese population; 3) Permanent residents, who living in those regions ≥ 5 years. **Exclusion criteria:** 1) Pregnant women; 2) Those who suffered from severe diseases such as hepatic cirrhosis, chronic renal failure or evident cardiac insufficiency; 3) Within three months, individuals who received medicines influencing thyroid function or hormones, such as iodine, amiodarone, somatostatin and glucocorticoidv. During the recruitment phase, a total of 2767 residents were invited to participate by examination notices or home visits. In total, 2720 subjects signed the consent form and agree to participate in the survey. After exclusion of 2 individuals for whom demographic information was incomplete and 220 for whom data on BMD were unfinished. Finally, 2,498 eligible individuals were included in the data analyses.

Ethical standards

All participants gave informed consents before recruited in the study. Study protocol was in accordance with the principles of the Helsinki Declaration II and our study was approved by Ethics Committee of the school of The First Hospital of China Medical University and the Institutional Review Board of the Sun Yat-sen Memorial Hospital affiliated Sun Yat-sen University (2014) [3].

Data collection

A standard questionnaire was used to collect information about lifestyle factors, medical history, sociodemograhpic characteristics and family history. And a variety of physical examination procedures involving general examination such as height, weight, waistline, body fat, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and laboratory examination including the levels of Total Cholesterol (TC), Triglycerides (TG), High-density Lipoprotein Cholesterol (HDL-C) and Low-density Lipoprotein Cholesterol (LDL-C) have been carried out for each participant. Measurements of laboratory hormones were performed with an autoanalyzer (Beckman CX-7 Biochemical Autoanalyser, Brea, CA, USA). Venous blood samples were collected and stored at -70°C for laboratory tests after an overnight fasting of at least 10 h.

Location was divided into two areas (rural and urban). Smoking and drinking were classified as "yes" (former or current) and "no" (never). The habit of nap and milk were divided into "yes"(own the habit past or now) and "no"(never). The dietary fruit, Vitamin D and calcium were recorded as low and high. The low frequency defined as ≤ 1 times/week or never and the high level was defined as ≥ 2 times/week. And the frequency of dietary fruit, Vitamin D and calcium were collected by subjects self-reported when asked by staff. Erectile dysfunction is defined as the inability to attain or maintain a penile erection sufficient to permit successful sexual intercourse. The presence study collected the information about erectile dysfunction by self-reported. The questionnaire for men included a self-assessment question: "Can you are able to get and keep an erection that is firm enough for satisfactory sexual activity?", with the response categories being "yes", "no" and "I would rather not answer this question".

Repeated blood pressure measurements were performed by a same observer three times with a 5 min interval. All the data obtained from an automated electronic device (OMRON, Omron Company, China). Body weight (kg) and height (cm) were measured in light clothing with no shoes, and were measured twice during the examination. Body mass index (BMI, kg/m^2) was calculated as weight (kg) divided by height squared (m^2). Neck circumference (NC, cm) was measured as the subject remaining standing and the head in the horizontal plane position, with a measuring tape along the inferior margin of the laryngeal prominence and perpendicular to the long axis of the neck, the circumferences were recorded to within 0.1 cm. Waist circumference (WC, cm) was measured to the nearest 0.1 cm at the umbilicus. Hip circumference (cm) at the level of maximum extension of the buttocks and the minimal circumference were recorded to the nearest 0.1 cm.

One Metabolic Equivalent (MET) is defined as the resting metabolic rate, that is, the amount of oxygen consumed while sitting at rest, approximately 3.5 ml O_2 per kg body weight*min. The information of Physical activity for all the participants obtained via the questionnaires, including the frequency per week, the average duration for each exercise and the type of physical activity. To estimate total energy expenditure from physical activity, the formulas of MET coefficient of activity*frequency (times per week)*duration (minutes per time) was used to calculated for each activity. Using the compendium of physical activities (http://links.lww.com/MSS/A82), which presents the 2011 update codes that can be used to identify the MET values for associated physical activities. METs per hour used for activities were: 7.0 for jogging, swimming and playing ball games, 6.0 for doing exercise in gym, 5.0 for dancing, 4.5 for qi gong and tai chi, 4.0 for biking, 3.5 for housework and 3.0 for walking. Finally, MET scores was divided into four groups by quartile: ≤ 630 MET-min/week, 631-1050 MET-min/week, 1051-1470 MET-min/

week and ≥ 1471 MET- min/week.

Diagnosis of osteoporosis

BMD at root bone for participants was used to diagnose osteoporosis in our study. BMD of the root bone was measured using clinical ultrasound bone densitometer (Sahara Clinical Bone Sonometer, 35 Crosby Drive, Bedford, Hologic, Inc, USA) according to standard protocol. According to the World Health Organization diagnostic criteria [19], osteoporosis was defined as BMD 2.5 standard deviations or more below the mean value for young adults (T score ≤ -2.5). What should be point out was that the most widely used technique to measure BMD is by X-ray absorptiometry (DXA), but because of the increasing demand for bone densitometry services, alternative cheaper technologies such as quantitative ultrasound have been used in recurrent years. Quantitative ultrasound as effectively as DXA in measurements of BMD for bone densitometry studies had been verified [20-22]. Our study is a type of epidemiological investigation and ultrasound bone densitometer would offer more convenient and less damage.

Statistical analysis

All data was entered into the double-track system of EpiData 3.0 software (EpiData Association, Odense Denmark) and verified consistency of result. Statistical analyses were performed using the SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA) and the R statistical programming language (version 3.1.4). Continuous variables with normal distribution were expressed as means ± Standard Deviation (SDs) and compared by Student's *t*-test. Continuous variables with non-normal distribution were presented as median (25th to 75th percentiles) and compared by Mann-Whitney U test or Kruskal-Wallis test. Binary and categorical data were described as frequency and percentage and compared using Pearson's χ^2 test or Fisher exact test when appropriate. Univariate and multivariate logistic regression models were used to obtain crude and adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of the association between each factor and osteoporosis. To build the multiple logistic regression model, we selected variables with clinical significance and all the association factors with $P \leq 0.05$ at the univariable level. In this study, Propensity Score (PS) matching analysis was used to control for potential confounding and to achieve balance. PS matching procedure was according to the "Propensity score matching in R" and variables potentially affecting the outcomes were assigned propensity score after logistic regression analysis in MatchIt packages. PS matching relied on a 1:1 nearest-neighbor procedure. Receiver Operating Characteristic (ROC) curve was used to evaluate the predictive value of logistic regression model of total population. Area Under the Curve (AUC) was used to evaluate the "overall diagnostic accuracy" of the test in relation to osteoporosis. All statistical tests were two-sided, and *P*-value were considered significant.

Results

Basic clinical and biochemical characteristics of the study population

A total of 2498 subjects (1082 male and 1416 female), 417 osteoporosis cases, 2081 non-osteoporosis cases were included in this study. In the group of osteoporosis, the median age was 58years (46~68years), and the median age was 43years (31~45years) in the non-osteoporosis group, osteoporosis subjects were significantly older than those with non-osteoporosis (P<0.001) and the same trend had been found in male population and female population. Compared with non-osteoporosis subjects, those who with osteoporosis had significantly higher body fat, waistline circumference, SBP, DBP, TC and LDL-C (P<0.05) in total population and sex-groups population (male population and female population). In addition, compared with non-osteoporosis subjects, those with osteoporosis presented with lower height, weight and neck circumference in all the groups (P<0.001). The clinical and biochemical characteristics according to osteoporosis status are summarized in Table 1.

Association of subjects characteristics with risk of osteoporosis

Among the 2498 subjects with BMD data, 417 (16.69%) were osteoporosis. The number of osteoporosis subjects in the rural group was higher than urban group (279, 22.0% *vs.*134, 11.3%, P<0.001). In addition, osteoporosis occurred in 30.0% in the low education population, 15.1% in the median education and 6.3% in the high education population. The distributions of other characteristics are showed in Table 2. The logistic regression modeling was used to explore the association of characteristics with risk of osteoporosis. As the results, location, higher education, habit of nap, habit of egg, frequency of fruit and vitamin D, and MET scores were statistically significant factors associated with osteoporosis. However, the level of family income, smoking, drinking and habit of milk showed no association

Table 1. The clinical characteristics of total population, male population and female population

Type	Total population (N=2498)		Male (N=1082)		Female (N=1416)	
	Osteoporosis (N=417)	Non-osteoporosis (N=2081)	Osteoporosis (N=134)	Non-osteoporosis (N=948)	Osteoporosis (N=283)	Non-osteoporosis (N=1133)
Age (years)	58 (46~68)	43 (31~54)**	51 (42~64)	43 (30~56)**	60 (51~70)	43 (32~53)**
Height (cm)	156.0 (151.4~162.5)	160.4 (155.0~167.3)**	165.4 ± 7.6	167.5 ± 6.3**	153.4 (150.0~157.2)	156.0 (152.1~159.5)**
Weight (kg)	57.0 (50.0~64.9)	60.0 (53.0~68.5)**	64.3 (56.0~72.1)	66.0 (59.5~73.5)*	54.0 (48.4~61.1)	55.0 (49.5~61.0)
BMI (kg/m²)	23.2 (21.0~25.5)	23.1 (20.8~25.7)	23.5 (21.0~25.4)	23.8 (21.2~26.1)	23.1 (20.9~25.5)	22.5 (20.4~25.3)
Body fat(%)	30.1 (25.5~34.8)	27.3 (23.1~31.9)**	25.3 (22.2~28.0)	24.3 (20.1~27.7)	32.3 (27.2~37.5)	30.3 (25.8~33.8)**
Neck circumference (cm)	33.0 (31.0~35.0)	34.3 (31.9~37.0)**	36.0 (34.0~38.0)	37.0 (35.3~39.0)**	31.7 (30.0~33.9)	32.0 (30.7~34.0)*
Waistline circumference (cm)	84.0 (76.0~90.0)	81.0 (73.5~89.0)**	86.0 (77.9~91.5)	85.0 (77.1~91.5)	83.0 (75.9~89.4)	78.0 (71.0~86.0)**
Hipline (cm)	93.9 (89.1~98.5)	94.2 (90.0~99.0)	94.5 (90.0~99.0)	95.3 (91.2~100.0)	93.2 (89.0~98.2)	93.0 (89.0~98.0)
SBP (mmHg)	135.0 (121.0~149.0)	126.0 (116.0~139.0)**	137.0 (125.0~149.0)	130.0 (121.0~143.8)**	133.0 (119.0~150.0)	122.0 (112.0~135.0)**
DBP (mmHg)	77.0 (69.0~85.0)	75.0 (68.0~83.0)*	81.0 (75.0~89.0)	77.0 (70.0~86.0)**	75.0 (67.0~82.0)	73.0 (66.0~80.0)
Heart-rate (times/min)	84.0 (75.0~92.0)	82.0 (75.0~90.0)	83.0 (73.0~93.0)	80.5 (73.0~89.0)	84.0 (75.0~92.0)	83.0 (76.0~91.0)
TC (mmol/L)	5.8 (4.9~6.6)	5.3 (4.7~6.1)**	5.7 (4.8~6.4)	5.4 (4.7~6.0)*	5.9 (4.9~6.7)	5.3 (4.6~6.1)**
TG (mmol/L)	1.2 (0.8~1.9)	1.1 (0.7~1.7)	1.3 (0.9~2.1)	1.4 (0.9~2.1)	1.1 (0.7~1.8)	0.9 (0.6~1.4)**
LDL-C (mmol/L)	3.4 (2.7~4.1)	3.1 (2.5~3.7)**	3.4 (2.6~4.1)	3.1 (2.6~3.7)*	3.4 (2.8~4.2)	3.1 (2.5~3.8)**
HDL-C (mmol/L)	1.4 (1.2~1.7)	1.4 (1.2~1.6)	1.3 (1.1~1.5)	1.3 (1.1~1.5)	1.5 (1.3~1.7)	1.5 (1.3~1.7)
Alt (U/L)	16.0 (12.0~22.0)	17.0 (12.0~24.0)	20.0 (14.0~28.3)	20.0 (15.0~29.0)	15.0 (11.0~20.0)	14.0 (11.0~20.0)
Cr (umol/L)	92.0 (83.0~108.0)	95.0 (84.0~108.0)	109.0 (99.0~119.0)	108.0 (100.3~116.0)	86.0 (80.0~95.0)	85.0 (79.0~92.0)*

Data were means ± standard deviation(SD) for normal distribution variables and medians (interquartile ranges) for skewed variables
*P<0.05 and **P<0.001 compared with osteoporosis group in total population, male population and female population
BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TC: Total Cholesterol; TG: Triglycerides; LDL-C: Low-Density Lipoprotein Cholesterol; HDC-C: High-Density Lipoprotein Cholesterol; Alt: Alanine Aminotransferse; Cr: Creatinine

with osteoporosis. All of the OR and 95%CI were adjusted by sex and age.

To make the study more accurate, we divided the total population into two groups by sex. As the results showed in male population, rural group have more risk to be osteoporosis than urban group. Comparing to the low education, median and high education have low risk to be osteoporosis. Owning the habit of nap was association with low risk of osteoporosis (P=0.027). The risk of osteoporosis in high frequency of fruit reduced to 61% than low frequency fruit group. The high level of MET scores was a association protection factor for risk of being osteoporosis. The other characteristics had not been found association with osteoporosis in this study. All of the ORs and 95%CI in male population were adjusted by age.

In the female population, location, habit of nap, frequency of fruit was not related to osteoporosis, what were different from the total and male population. High education had low risk of osteoporosis. The population had the high frequency of vitamin D and high levels of MET scores were association with low risk of osteoporosis. Besides, what should been marked was the risk of osteoporosis in dinking population is lower than in non-drinking population. ORs and 95%CI were adjusted by age. The detailed results are showed in Table 2.

Multivariate logistic regression analysis of OR and 95%CI of osteoporosis in three groups population

We performed multivariate logistic regression analysis to explore the independent risk factor for osteoporosis in total population. Demographic characteristics, life style and lipid parameters selected at the unadjusted model with P<0.05 were included in multivariate logistic regression analysis.

In total population, six influencing variables were

Table 2. ORs and 95%CIs of subjects characteristics for osteoporosis in univariate logistic regression

Type	Total population (N=2498)				Male population (N=1082)				Female population (N=1416)			
	N	Osteoporosis	*OR (95%CI)	*P*	N	Osteoporosis	#OR (95% CI)	*P*	N	Osteoporosis	#OR (95% CI)	*P*
Location												
City	1189	134 (11.3)	1.00	**<0.001**	652	52 (8.0)	1.00	<0.001	537	82 (15.3)	1.00	0.062
Country-side	1268	279 (22.0)	**1.65 (1.30-2.11)**		406	80 (19.7)	**2.47 (1.67-3.64)**		862	199 (23.1)	1.35 (0.99-1.84)	
Education												
Low	686	206 (30.0)	1.00	**<0.001**	176	39 (22.2)	1.00	**0.004**	510	167 (32.7)	1.00	0.076
Median	1094	165 (15.1)	0.78 (0.59-1.01)	0.062	527	72 (13.7)	0.68 (0.43-1.10)	0.113	567	93(16.4)	0.87 (0.62-1.21)	0.403
High	711	45 (6.3)	**0.43 (0.29-0.66)**	**<0.001**	374	22 (5.9)	**0.34 (0.18-0.65)**	**0.001**	337	23 (6.8)	**0.52 (0.30-0.92)**	**0.023**
Income												
Low	669	120 (17.9)	1.00	0.855	255	29 (11.4)	1.00	0.750	414	91 (22.0)	1.00	0.911
Median	1028	183 (17.8)	1.08 (0.82-1.42)	0.578	419	55 (13.1)	1.18 (0.73-1.92)	0.497	609	128 (21.0)	1.06 (0.76-1.48)	0.740
High	723	101 (14.0)	1.06 (0.77-1.44)	0.733	368	44 (12.0)	1.20 (0.72-2.00)	0.492	355	57 (16.1)	0.99 (0.66-1.48)	0.941
Smoking												
No	1974	338(17.1)	1.00	0.079	581	59 (10.2)	1.00	0.056	1393	279 (20.0)	1.00	0.660
Yes	517	79 (15.3)	1.38 (0.96-1.98)		498	75 (15.1)	1.44 (0.99-2.09)		19	4 (21.1)	0.76 (0.23-2.57)	
Drinking												
No	1237	275 (22.2)	1.00	0.062	300	39 (13.0)	1.00	0.200	937	236 (25.2)	1.00	<0.001
Yes	1253	140 (11.2)	0.78 (0.61-1.01)		781	95 (12.2)	1.32 (0.86-2.01)		472	45 (9.5)	**0.52 (0.36-0.75)**	
Habit of nap												
No	1052	203 (19.3)	1.00	**0.024**	404	60 (14.9)	1.00	**0.027**	648	143 (22.1)	1.00	0.320
Yes	1433	213 (14.9)	**0.77 (0.62-0.97)**		674	74 (11.0)	**0.66 (0.45-0.95)**		759	139 (18.3)	0.87 (0.65-1.15)	
Habit of milk												
No	653	162 (24.8)	1.00	0.054	299	50 (16.7)	1.00	0.374	354	112 (31.6)	1.00	0.091
Yes	1836	252 (13.7)	0.79 (0.62-1.01)		778	83 (10.7)	0.83 (0.56-1.25)		1058	169 (16.0)	0.76 (0.56-1.04)	
Habit of egg												
0-3/week	1903	337 (17.7)	1.00	0.100	807	106 (13.1)	1.00	0.444	1096	231 (21.1)	1.00	0.199
4-6/week	492	71 (14.4)	0.93 (0.69-1.25)	0.621	226	25 (11.1)	0.94 (0.59-1.50)	0.789	266	46 (17.3)	0.93 (0.63-1.36)	0.698

≥ 7/week	95	9 (9.5)	**0.46 (0.22-0.94)**	**0.034**	46	3 (6.5)	0.46 (0.14-1.53)	0.207	49	6 (12.2)	0.43 (0.17-1.09)	0.075
Frequency of fruit												
Low	543	119 (21.9)	1.00	**0.008**	292	47 (16.1)	1.00	**0.014**	251	72 (28.7)	1.00	0.556
High	1943	298 (15.3)	**0.71 (0.55-0.91)**		782	87 (11.1)	**0.61 (0.41-0.90)**		1161	211 (18.2)	0.90 (0.63-1.28)	
MET scores												
≤ 630	504	102 (20.2)	1.00	**0.006**	186	30 (16.1)	1.00	0.170	318	72 (22.6)	1.00	**0.031**
631-1050	412	55 (13.3)	**0.63 (0.43-0.91)**	**0.015**	184	24 (13.0)	0.77 (0.43-1.40)	0.397	228	31 (13.6)	**0.55 (0.33-0.90)**	**0.019**
1051-1470	456	55 (12.1)	**0.65 (0.44-0.94)**	**0.024**	234	26 (11.1)	0.71 (0.40-1.27)	0.252	222	29 (13.1)	0.61 (0.36-1.02)	0.058
≥ 1471	399	37 (9.3)	**0.51 (0.34-0.78)**	**0.002**	218	14 (6.4)	**0.46 (0.23-0.91)**	**0.026**	181	23 (12.7)	**0.53 (0.30-0.92)**	**0.024**
Frequency of Vitamin D												
Low	2336	404 (17.3)	1.00	**0.005**	1007	130 (12.9)	1.00	0.152	1329	274 (20.6)	1.00	**0.011**
High	120	9 (7.5)	**0.36 (0.18-0.74)**		54	3 (5.6)	0.42 (0.13-1.38)		66	6 (9.1)	**0.31 (0.13-0.76)**	
Frequency of calcium												
Low	2145	343 (16.0)	1.00	0.822	957	117 (12.2)	1.00	0.956	1188	226 (19.0)	1.00	0.793
High	333	70 (21.0)	1.04 (0.76-1.41)		117	16 (13.7)	0.98 (0.56-1.74)		216	54 (25.0)	1.05 (0.72-1.53)	

*OR (95%CI) were adjusted by sex and age (age was divided into three subgroups, ≤ 40 years, 41-60 years and ≥ 61years)
#OR (95%CI) were adjusted by age (age was divided into three subgroups, ≤ 40 years, 41-60years and ≥ 61years)
The low level education is belong to illiteracy and primary school; The median level education is belong to secondary school and high school; The high level education is belong to university degree and postgraduate degree
The low level income is belong to ≤ 10,000yuan per year for family, the median level income is belong to 10,000-50,000yaun per year for family and the high level is belong to ≥ 50,000 yuan per year for family
Frequency of fruit were defined as high and low, high level was defined as ≥ 1 time per week, and the low level was defined as <1time per week or never

included: age, education, frequency of vitamin D, MET scores, weight and waistline. In addition, Neck circumference and the level of TC showed the trend of being predictors of osteoporosis. People ≥ 40 years and the high level of waistline were the independent risk factor of osteoporosis. However, high education, high frequency of vitamin D, high MET scores and high weight were the independent protection factors. No significant relationships between other parameters were observed.

In male population, weight ≥ 68.1kg was an independent prevention factor (OR=0.16, 95%CI: 0.04-0.61, *P*=0.007) and rural location and erectile dysfunction were independent associated with high risk for osteoporosis, with odds ratios of 1.86 (95%CI: 1.01-3.43, *P*=0.047) and 2.61 (95%CI: 1.33-5.12, *P*=0.005), respectively. Age tented to be positive associated with osteoporosis development, although statistically insignificant (*P*=0.078).

In female population, the results from the multivariate regression test showed that age, menopause, waistline were independent risk factors but frequency of Vitamin D, MET scores and TG were independent protection factors. Drinking, TC and neck circumference tended to be protection factors associated with osteoporosis development, although statistically insignificant (*P*=0.054, *P*=0.056 and *P*=0.074, respectively). Firstly, Older participants were more likely to have osteoporosis than young (OR=6.38, 95%CI: 2.42-16.83, *P*<0.001) and participants who showed menopause were associated with a higher risk to be osteoporosis than those were non-menopause (OR=2.87, 95%CI:1.51-5.46, *P*=0.001). Secondly, participants whose high levels

Table 3. The multivariate OR and 95%CI for total population, male population and female population

Population	Type	β	SE	Wald	OR (95%CI)	*P*
Total population	**Age (≤ 40 years *vs.* 14-60years)**	0.76	0.24	10.20	**2.13 (1.34-3.39)**	**0.001**
	Age (≤ 40 years *vs.* ≥ 61 years)	1.64	0.29	32.76	**5.13 (2.93-8.98)**	**<0.001**
	Education (Low *vs.* High)	-0.60	0.29	4.14	**0.55 (0.31-0.98)**	**0.042**
	Frequency of Vitamin D (Low *vs.* High)	-1.27	0.45	7.89	**0.28 (0.12-0.68)**	**0.005**
	MET scores (≤ 630 *vs.* 631-1050)	-0.34	0.21	2.76	0.71 (0.47-1.06)	0.097
	MET scores (≤ 630 *vs.* 1051-1470)	-0.44	0.21	4.30	**0.65 (0.43-0.98)**	**0.038**
	MET scores (≤ 630 *vs.* ≥ 1471)	-0.61	0.23	6.86	**0.55 (0.35-0.86)**	**0.009**
	Weight (≤ 52.0 vs. 52.1-59.5)	-0.77	0.27	7.86	**0.47 (0.27-0.79)**	**0.005**
	Weight (≤ 52.0 vs. 59.6-68.0)	-0.90	0.34	7.01	**0.41 (0.21-0.79)**	**0.008**
	Weight (≤ 52.0 vs. ≥ 68.1)	-1.29	0.44	8.48	**0.28 (0.17-0.66)**	**0.004**
	Neck circumference (≤ 31.8 *vs.* 31.9-34.0)	-0.25	0.24	1.12	0.78 (0.49-1.24)	0.289
	Neck circumference (≤ 31.8 *vs.* 34.1-37.0)	-0.53	0.29	3.24	0.59 (0.33-1.05)	0.072
	Neck circumference (≤ 31.8 *vs.* ≥ 37.1)	-0.72	0.37	3.76	**0.49 (0.24-1.01)**	**0.053**
	Waistline (≤ 74.1 *vs.* 74.2-82.0)	0.68	0.26	6.92	**1.98 (1.19-3.29)**	**0.009**
	Waistline (≤ 74.1 *vs.* 82.1-89.2)	0.93	0.33	7.97	**2.53 (1.33-4.80)**	**0.005**
	Waistline (≤ 74.1 *vs.* ≥ 89.3)	0.96	0.40	5.85	**2.60 (1.20-5.64)**	**0.016**
	TC (≤ 4.70 *vs.* 4.71-5.38)	-0.27	0.26	1.02	0.77 (0.46-1.29)	0.314
	TC (≤ 4.70 *vs.* 5.39-6.15)	-0.51	0.31	2.76	**0.60 (0.33-1.10)**	**0.097**
	TC (≤ 4.70 *vs.* ≥ 6.16)	-0.07	0.35	0.04	0.94 (0.47-1.85)	0.849
Male population	Age (≤ 40 years *vs.* 14-60 years)	0.43	0.36	1.43	1.53 (0.76-3.07)	0.232
	Age (≤ 40 years *vs.* ≥ 61 years)	0.84	0.47	3.12	**2.31 (0.91-5.84)**	**0.078**
	Location (City *vs.* Countryside)	0.62	0.31	3.96	**1.86 (1.01-3.43)**	**0.047**
	Weight (≤ 52.0 vs. 52.1-59.5)	-0.87	0.59	2.22	0.42 (0.13-1.32)	0.136
	Weight (≤ 52.0 vs. 59.6-68.0)	-0.93	0.59	2.48	0.40 (0.12-1.25)	0.115
	Weight (≤ 52.0 vs. ≥ 68.1)	-1.83	0.68	7.17	**0.16 (0.04-0.61)**	**0.007**
	Erectile dysfunction (No *vs.* Yes)	0.96	0.34	7.82	**2.61 (1.33-5.12)**	**0.005**
Female population	**Age (≤ 40 years *vs.* 14-60years)**	0.69	0.39	3.22	**2.00 (0.94-4.25)**	**0.073**
	Age (≤ 40 years *vs.* ≥ 61 years)	1.85	0.50	14.03	**6.38 (2.42-16.83)**	**<0.001**
	Drinking (No *vs.* Yes)	-0.50	0.26	3.70	**0.61 (0.37-1.01)**	**0.054**
	Frequency of Vitamin D (Low *vs.* High)	-1.44	0.59	6.00	**0.24 (0.08-0.75)**	**0.014**
	Menopause (No *vs.* Yes)	1.05	0.33	10.27	**2.87 (1.51-5.46)**	**0.001**
	MET scores (≤ 630 *vs.* 631-1050)	-0.59	0.29	4.15	**0.56 (0.32-0.98)**	**0.042**
	MET scores (≤ 630 *vs.* 1051-1470)	-0.61	0.29	4.46	**0.54 (0.31-0.96)**	**0.035**
	MET scores (≤ 630 *vs.* ≥ 1471)	-0.87	0.32	7.21	**0.42 (0.22-0.79)**	**0.007**
	Neck circumference (≤ 31.8 *vs.* 31.9-34.0)	-0.44	0.27	2.68	0.64 (0.38-1.09)	0.102
	Neck circumference (≤ 31.8 *vs.* 34.1-37.0)	-0.62	0.34	3.19	**0.54 (0.28-1.06)**	**0.074**
	Neck circumference (≤ 31.8 *vs.* ≥ 37.1)	-1.40	0.66	4.50	**0.25 (0.07-0.90)**	**0.034**
	Waistline (≤ 74.1 *vs.* 74.2-82.0)	0.64	0.33	3.80	**1.90 (1.00-3.64)**	**0.051**
	Waistline (≤ 74.1 *vs.* 82.1-89.2)	1.23	0.41	8.97	**3.41 (1.53-7.62)**	**0.003**
	Waistline (≤ 74.1 *vs.* ≥ 89.3)	0.67	0.47	2.03	1.96 (0.78-4.93)	0.154
	TC (≤ 4.70 *vs.* 4.71-5.38)	-0.25	0.38	0.45	0.78 (0.37-1.62)	0.501
	TC (≤ 4.70 *vs.* 5.39-6.15)	-0.87	0.46	3.65	**0.42 (0.17-1.02)**	**0.056**
	TC (≤ 4.70 *vs.* ≥ 6.16)	-0.17	0.51	0.11	0.84 (0.31-2.29)	0.738
	TG (≤ 0.74 *vs.* 0.75-1.11)	-0.21	0.30	0.50	0.81 (0.45-1.46)	0.481
	TG (≤ 0.74 *vs.* 1.12-1.76)	-0.66	0.33	3.89	**0.52 (0.27-0.99)**	**0.049**
	TG (≤ 0.74 *vs.* ≥ 1.77)	-0.35	0.36	0.96	0.70 (0.35-1.42)	0.327

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LDL-C: Low-Density Lipoprotein Cholesterol; TC: Total Cholesterol
MET, Height, Weight, Body fat, Neck circumference, Waistline, SBP, DBP, LDL-C and TC were grouped by quartile

of MET scores were associated with a lower risk of osteoporosis. In addition, participants who own the habit of drinking showed the trended to be lower risk for the development of osteoporosis than those with non-drinking (OR=0.61, 95%CI:0.37-1.01, *P*=0.054). The detailed results for other variables have been showed in Table 3.

Association of bone mineral density with erectile

dysfunction and drinking after PS matching in male and female population

To further investigate the relationship between bone mineral density and erectile dysfunction in male population and the association of bone mineral density and drinking in female population, PS matching analysis was used to control for potential confounding from imbalance in clinical characteristics. In male population, the independent factors including age, location and weight as covariates were used to influence the probability (i.e. propensity score) of osteoporosis. Simultaneously, in female population, the independent factors including age, frequency of vitamin D, menopause, MET scores, neck circumference, waistline, TC and TG were selected in a logistic regression model for PS matching analysis to influence the probability (i.e. propensity score) of osteoporosis.

In male population, the characteristics of the PS matching results was no differences in osteoporosis and non-osteoporosis about age, location and weight, but except erectile dysfunction. In the group of aged 40 years or lower, the median of BMD in non-erectile dysfunction was -2.30, and -2.90 for erectile dysfunction group (*P*=0.026). In the group aged from 41 to 61 years, the level of BMD in erectile dysfunction was lower than in non-erectile dysfunction (-2.87 *vs.* -1.88, *P*=0.022). However, in the group of male population aged ≥ 61 years, the level of BMD in erectile dysfunction and non-erectile dysfunction no statistical differences had been observed in this study (*P*=0.335). Finally, we presented the association of erectile dysfunction and BMD in the total male population, the results showed that the level of BMD in erectile dysfunction was lower than that in non-erectile dysfunction (-2.34 *vs.* -1.82, *P*=0.002) (Figure 1).

In female population, we divided the participants into three groups according to the frequency of drinking, including never, occasionally and ≥ 3times/week in female population. BMD in drinking population is higher than that in non-drinking population (-1.824 *vs.*-2.223, *P*=0.015), and the BMD in occasionally drinking population was higher than that in never drinking population (-1.793 *vs.* -2.223, *P*=0.010) (Figure 2).

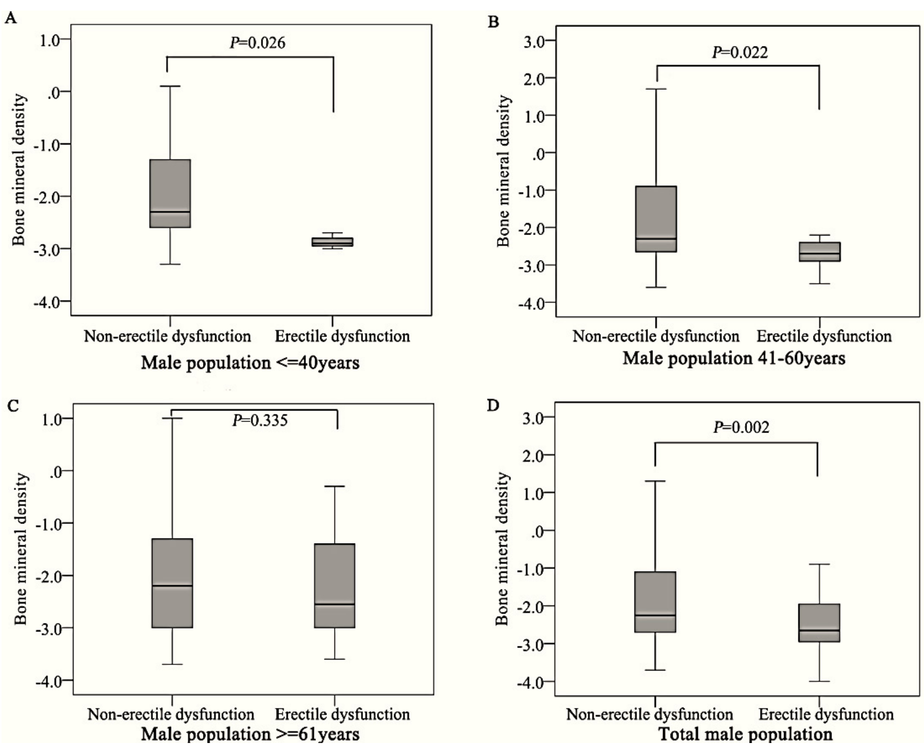

Figure 1: The relationship of erectile dysfunction and bone mineral density (BMD) in four groups divided by age in male population. (A) male population ≤ 40 years, the median of BMD in non-erectile dysfunction group is -2.30 (-2.60~-1.3) and in erectile dysfunction is -2.90, the level of BMD in erectile dysfunction was lower than in non-erectile dysfunction (*P*=0.026); (B) Male population, age from 41 years to 60 years, the level of BMD in erectile dysfunction group was lower than that in non-erectile dysfunction too (-2.867 vs. -1.878, P=0.022); (C) Male population aged ≥ 61 years, the level of BMD in two group no statistical differences had been observed in this study (P=0.335); (D) Finally, we wxplored the association of erectile dysfunction and BMD in total male population, the level of BMD in erectile dysfunction group was lower than in non-erectile dysfunction (-2.342 vs. -1.815, P=0.002).

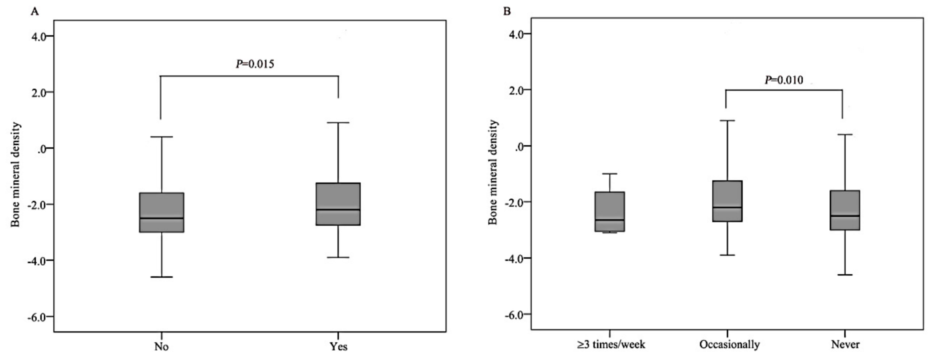

Figure 2: The relationship of drinking and Bone Mineral Density (BMD) in female population. (A) BMD in drinking population is higher than in non-drinking (*P*=0.015), (B) BMD in occasionally drinking population is higher than never drinking population (*P*=0.010).

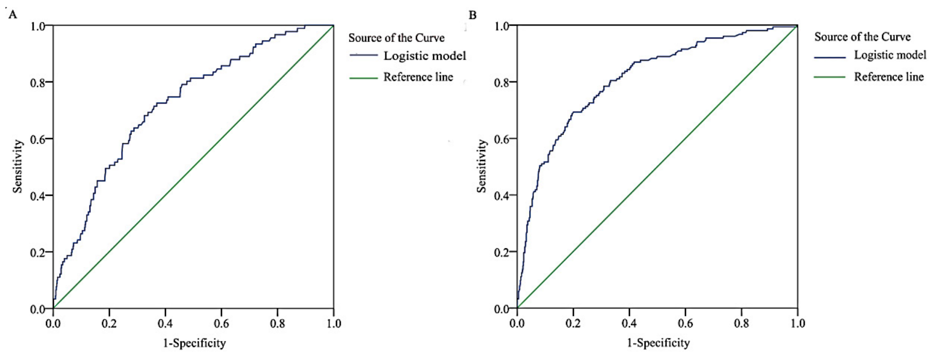

Figure 3: ROC curve analysis for the logistic model in total population for osteoporosis prediction. (A) ROC curve analysis for the logistic model in total population for osteoporosis prediction in the male population; (B) ROC curve analysis for the logistic model in total population for osteoporosis prediction in the female population.

Using the ROC curve to evaluate the predictive value of the logistic regression model

ROC curve was used to evaluate the predictive value of logistic regression model of total population. The status of osteoporosis in male and female population was used as the "gold standard" for predicting models and ROC curve analysis, as the results shown in Table 3. The independent factors for osteoporosis in total population including age, education, frequency of vitamin D, MET scores, weight, neck circumference, waistline and TC. In male and female population, osteoporosis represented the end-point with a status of 1 versus non-osteoporosis with a status of 0. Stepwise multiple logistic regressions were performed to assess the variables significantly linked to the probability of osteoporosis. The area under ROC curve for the male population and female population were 0.721 (± 0.027, P<0.001) and 0.809 (± 0.020, P<0.001) under the logistic regression model of total population. Sensitivity was 68.1% and specificity was 67.5% in male population, and sensitivity reached 69.3% and specificity reached 79.9% in female population as shown by the ROC curves (Figure 3).

Discussion

Similar to other studies [23-28], we found that high education, high frequency of vitamin D intake, high level of MET scores, the high level of weight, high level of neck circumference and high level of TC were association with reducing risk of osteoporosis and high level of waistline was association with increasing risk of osteoporosis. Elderly was an independent risk factors for the development of osteoporosis and advancing age contributes to fracture risk independently of BMD [15]. High education is a marker for low risk osteoporosis [29]. Patients with high education levels were more knowledgeable about osteoporosis and awareness of prevention, easier to understand how to maintain good habit of lifestyle and enhance the function of body. Furthermore, vitamin D and exercise has been identified as possible causes of protection of bone mineral density loss [24]. Multiple studies [30-32] demonstrate adequate vitamin D intake and health exercise ultimately reduces the risk of osteoporosis, the former provides sufficient levels for bone density maintenance and bone formation, and supplementation has long been considered important for osteoporosis prevention; the latter can improve posture, balance, strength and agility and decrease bone loss to prevent osteoporosis.

Increased weight level and neck circumference were association with decreased osteoporosis risk. The possible mechanism are as follow [33]: Higher weight and neck circumference with more mechanical load which represents an osteogenetic stimulus and high weight and circumference with more fat mass which represent the place of aromatization of androgen hormones into estrogens. Estrogens were important protection factors for the development of osteoporosis [34]. The fact that neck circumference closely related with body fat mass had been confirmed in studies [35-37]. However, different from weight and neck circumference, the results showed that the high levels waistline were risk factors for osteoporosis. Together these results reinforce that osteoporosis risk is lower in individuals with high weight, high neck circumference and low waistline. Studies [38-40] showed that high level of waistline seems to be an important marker of low osteoporosis risk, and other study [41] showed opposite. In the literature, waistline has been considered as a simple screening tool for center obesity and positively associated with visceral fat. Our study suggested that the effect of waistline on bone mineral density depend on fat distribution. The central obesity subjects with higher osteoporosis risk compared with general obesity. Therefore, large cohort and mechanism studies are needed to define waistline differences in osteoporosis.

The association between bone mineral density and serum lipid has showed in some studies [38,42,43]. In a South Korean population-based study of 355 postmenopausal and 375 premenopausal women it was showed that TC and LDL-C were inversely correlated with BMD [44]. Furthermore, LDL-C and HDL-C have been shown to be inversely and positively correlated with BMD in both men and women, respectively. However, in some studies, TG and HDL-C were found to be correlated with BMD, but not for TC and LDL-C. Our results showed that only high level of TC is predictor of low osteoporosis risk, and the relationship between other serum lipids and osteoporosis have not been found yet. Despite the controversy, the results suggest that serum lipids have roles in the manifestation of osteoporosis.

Significant association between erectile dysfunction and osteoporosis has been indentified in our study and this finding is consistent with the others. Studies [45,46] investigated the association of erectile dysfunction with osteoporosis and reported that the men with erectile dysfunction had low BMD and were at higher risk of osteoporosis than were their healthy counterparts. Erectile dysfunction primarily affects men over 40 years of age and what have been identified that osteoporosis affects an enormous number of people and its prevalence will increase as the population ages. Our study demonstrated that the relationship between erectile dysfunction and osteoporosis were different according to age groups. In the group of participants aged 40 years or lower, the level of BMD in non-erectile dysfunction subjects is higher than that in erectile dysfunction individuals, the same phenomenon have been observed in participants aged from 41 to 60 and total man population, but not for subjects age 61 years or more. Our results suggest that the association of erectile dysfunction and osteoporosis is more closely in younger population than that in elderly.

It is surprising in our study that women participants with habit of drinking had a low likelihood of developing osteoporosis, which is inconsistent with the report that avoidance of alcohol intake are the universal recommendation for reducing the incidence of osteoporosis [47-49]. As shown in our results, drinking was a protective factor for osteoporosis only in female population based on adjusting the independent influence factors showed in multiple logistic regression models using PS matching. Similarly, Heidi Dl study shown that moderate-drinking have better physical function and lower risk of osteoporosis compared with non-drinking. In addition, a study for examining the relationship between bone mineral density and alcohol consumption in Korean menopause women shown that mean bone mineral density of light drinkers was greater than those of non-drinkers and heavy drinkers. However, alcohol abuse has been identified as the risk factor for osteoporosis in some other studies. The protective effect of occasionally drinking in women population may be related to stimulate estrogen secretion and the mechanism should be studied deeply.

At the end of paper, we used ROC curve to evaluate the predictive value of logistic regression model of total population. We verified the predictive value of the logistic model of total population in male and female population and the predictive value of model is high in female and male population (ROC curve: 0.809 *vs.* 0.721; sensitivity: 69.3% *vs.* 68.1%; specificity: 79.9% *vs.* 67.5%). The association model can be used as guidelines to prevent osteoporosis. In addition, conditions of erectile dysfunction and menopause should be taken seriously in male population and female population, respectively.

To our knowledge, we have generated the largest and most comprehensive assessment of the relationship between lives related risk factor and osteoporosis so far in Southern China, Guangzhou. Propensity Score (PS) matching analysis was used to control for potential confounding and to achieve balance. Besides, receiver operating characteristic curve was used to evaluate the predictive value of logistic regression model of total population. We also found that erectile dysfunction associated osteoporosis in younger male population and drinking was a protective factor for osteoporosis only in female population. Our study also had limitations, as our analyses relied on cross section data, these findings should be interpreted cautiously and should not be considered as causal estimates of the impact of related lifestyle and metabolic factors on osteoporosis. The second major limitation was linked to outcome. The distinguish between osteoporosis and non-osteoporosis based on clinical ultrasound bone densitometer in root bone, which the accuracy is lower than dual energy X-ray absortiometry. But because the method of dual energy X-ray absortiometry can cause some radioactive injury, and not suitable for epidemiological investigation population. The method of clinical ultrasound bone densitometer is acceptable evaluated the level of BMD.

Conclusion

This study provides data on the risk of osteoporosis in total population, male population and female population. The risk for osteoporosis was significantly associated with age, vitamin D intake, MET scores, weight, neck circumference, waistline and TC in total population. In male population, osteoporosis was associated with age, weight and condition of erectile dysfunction. The results suggest that erectile dysfunction was associated with high risk of osteoporosis in male population. The osteoporosis risk factors in female population were similarly with total population, but there were two different points would be note, including drinking and menopause. Drinking was protection factor only in female population and the menopause was independent risk factor. Furthermore, we also evaluate the influencing value model of total population in male and female population, and the predictive value of logistic regression model is perfect. Our study lends support that some related lifestyle and metabolic factors may be the predictive factors for the development of osteoporosis and the underlying biological roles needed to reveal by further studies. The roles of fat distribution, erectile dysfunction, menopause and drinking in osteoporosis should be given more consideration in the clinical practice.

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Availability of Data and Materials

All data supporting the findings reported in this work are at the Sun Yat-sen Memorial Hospital, Sun Yat-sen University, but not available to the public. However, all data can be obtained from the authors upon reasonable request, with approval from the Sun Yat-sen Memorial Hospital ethics committee.

Authors' Contributions

YLL and LF supervised data generation and analysis, and drafted the manuscript. FWT, RM, WMC,ZJ, WC, TJY and ZXY were responsible for data collection. YL and XMT contributed to study design and interpreted the acquired data. All authors were involved in study conception and design, as well as data acquisition. All authors read and approved the final manuscript.

Ethics Approval and Consent Participate

The current study of human subjects was approved by the First Affiliated Hospital of China Medical University (201402005) and Sun Yat-sen Memorial Hospital, Sun Yat-sen University (2014) [33]. Written informed consent was obtained from each participant before enrolment.

Consent for Publication

Not applicable

Competing Interests

The authors declare that they have no competing interests.

Executive summary

Background: Several studies have investigated the risk factors for osteoporosis in China, but little is known about the situation of osteoporosis in Southern China in recent years. Our present study investigates the osteoporosis risk factors of total population, male population and female population in Southern Chinese community-based population, aiming to suggest more effects for prevention and control of osteoporosis.

Materials: A multistage stratified random cluster sampling design was used in this cross-sectional study conducted in 2015. Osteoporosis was defined as T scores ≤ -2.5 at root bone. Unconditional and multivariate logistic regression analysis was used to calculate Odds Ratios (ORs) and 95% Confidence Intervals (CIs). Propensity Score (PS) matching analysis and Receiver Operating Characteristic (ROC) curve were used to control potential confounding and evaluate the predictive value of prediction model, respectively.

Results: The estimated prevalence of osteoporosis in Southern China of Guangzhou was 16.69%. Osteoporosis was positively associated with age, education level, vitamin D intake, physical activity, weight, neck circumference, waistline and total cholesterol level in total population. Increased weight level was association with low risk of osteoporosis. Besides, erectile dysfunction subjects with low bone mineral density in male population and menopause was independent risk factor for development of osteoporosis in female population. What's more, occasional and moderate drinking was protective factor for osteoporosis only in female population. Our study suggests that the roles of fat distribution but not only for fat quantity should be taken seriously to explore the association with osteoporosis.

Conclusion: We observed a high prevalence of osteoporosis among the Southern China in Guangzhou City. Meanwhile, our study lends support that some related lifestyle and metabolic factors may be the association factors for the development of osteoporosis. Government and health department should take measures to improve people's awareness of osteoporosis and reduce the prevalence of osteoporosis in Southern China. Our results will provide latest scientific evidence for health policy formulating.

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