Heliyon 9 (2023) e21501

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Early risk assessment and prediction model for osteoporosis based on traditional Chinese medicine syndromes

Dan Liu [a], Zhijun Hu [a,*], Zhanying Tang [a], Pan Li [a], Weina Yuan [a], Fangfang Li [a], Qian Chen [a], Wen Min [b], Changwei Zhao [c]

[a] *Department of Rehabilitation Medicine, Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, 200032, China*

[b] *Department of Orthopedics, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, 210004, Jiangsu Province, China*

[c] *Department of Orthopedics, Affiliated Hospital of Changchun University of Chinese Medicine, Changchun, 130021, Jilin Province, China*

ARTICLE INFO

Keywords:
Osteoporosis
Risk factors
Prediction model
Adult
Traditional Chinese medicine (TCM) syndromes

ABSTRACT

Objective: To evaluate the risk factors of osteoporosis and establish a risk prediction model based on routine clinical information and traditional Chinese medicine (TCM) syndromes.

Methods: Adults aged 30–82 who lived in 12 grass-roots communities or rural towns in Shanghai, Jilin Province, and Jiangsu Province from December 2019 to January 2022 through a multi-stage sampling method were included in this study. The risk factors and risk prediction of osteoporosis in women and men were explored and established by univariate analysis and multivariate logistic regression model. ROC curve and Hosmer-Lemeshow goodness-of-fit test were used to evaluate the prediction model.

Results: A total of 3000 subjects including 2243 females (75 %) and 757 males (25 %) were included in this study. The logistic prediction model of osteoporosis in women was Logit (P) = −2.946 + 0.960 (age ≥50 years old) + 0.633 (BMI ≥24 kg/m^2) - 0.545 (daily exposure to sunlight >30 min) + 0.519 (no intake of dairy products) + 0.827 (coronary heart disease) + 0.383 (lumbar disc herniation) + 0.654 (no intake of calcium tablets and vitamin D) - 0.509 (insomnia) + 0.580 (flushed face and congested eyes) + 1.194 (thready and rapid pulse) + 1.309 (sunken and slow pulse). The logistic prediction model of osteoporosis in men was Logit (P) = −1.152–0.644 (daily exposure to sunlight >30 min) + 0.975 (no intake of calcium tablets and vitamin D) - 0.488 (insomnia). The area under the ROC curve (AUC) of female and male osteoporosis prediction models was 0.743 and 0.679, respectively. The Hosmer-Lemeshow goodness-of-fit test was >0.5.

Conclusions: There are some significant differences in risk factors between female and male patients with osteoporosis. The risk of osteoporosis are found to be associated with TCM syndromes, and osteoporosis risk prediction models based on routine clinical information and TCM syndrome is effective.

* Corresponding author. Department of Rehabilitation Medicine, Longhua hospital affiliated to Shanghai university of traditional Chinese medicine, No. 725, South wan ping road, Xu hui district, Shanghai, 200032, China.

E-mail address: hzjz1062@163.com (Z. Hu).

https://doi.org/10.1016/j.heliyon.2023.e21501
Received 16 June 2023; Received in revised form 19 October 2023; Accepted 23 October 2023
Available online 27 October 2023

1. Introduction

Osteoporosis is a metabolic bone disease characterized by reduced bone mass, microstructural degeneration, and fragility fractures [1]. Patients with osteoporosis do not manifest significant symptoms when it is not complex, but can contribute to fragility fractures, with serious consequences and even death [2]. A review has suggested that osteoporosis influences approximately 10 million Americans [3]. With the expansion of the aging population and the drastic changes in the lifestyle, the population with osteoporosis has also been growing [4]. Osteoporosis and its resulting fragility fractures already constitute a huge medical, public health, and economic burden worldwide and are recognized as a major public health problem [5].

The International Osteoporosis Foundation (IOF) clearly states that a healthy lifestyle can significantly reduce the risk of osteoporosis, therefore, the construction of a risk prediction model for osteoporosis is of great clinical significance for the early intervention of the corresponding patients [6]. Evidence has shown that bone density in early life, a healthy diet (especially adequate intake of calcium and vitamin D) and regular physical activity can help to determine a person's risk of osteoporosis [7].

Existing research for the exploration of the main clinical risk factors of osteoporosis has revealed that routine clinical information such as older age, gender (female susceptibility), race, heredity, previous fracture, malnutrition, alcohol consumption, current smoking, vitamin D deficiency, lack of exercise, as well as various drugs and medical barriers [8–10] are related to enhanced risk of osteoporosis. Given the large osteoporosis-affected population and the distinctive characteristics of traditional Chinese medicine (TCM) syndromes in China, the Development Plan of TCM Health Services (2015–2020) [11] also recommends performing a health risk assessment and intervention based on TCM, providing health management services with TCM characteristics.

The current study included adults aged 30–82 who lived in 12 grass-roots communities or rural towns in Shanghai, Jilin Province, and Jiangsu Province through a multi-stage sampling method. We aimed to explore the risk factors affecting osteoporosis in women and men and construct related prediction models to provide evidence-based medical evidence for early prediction of osteoporosis in a combination with the demographic information and TCM syndrome information.

2. Materials and methods

2.1. Study subjects and data collection

In our study, participants were recruited through a multi-stage sampling method. First, we randomly selected several cities from the northernmost and easternmost regions of China as primary sampling units. Then, within each selected city, we randomly chose specific neighborhoods or communities as secondary sampling units. Finally, within each neighborhood or community, eligible individuals were randomly selected as our study participants. Regarding the sample size, we used the PASS software to achieve a sufficient statistical power for our analyses (Supplementary material). Finally, this study recruited 3000 adults aged 30–82 years old from 12 grass-roots communities or rural towns in Shanghai City, Jilin Province, and Jiangsu Province from December 2019 to January 2022 on a voluntary basis. Data other than TCM syndromes were collected through questionnaires, while the TCM syndrome data was collected by two experienced TCM practitioners. In cases where there were differing opinions regarding a particular individual, a third senior TCM practitioner was involved for further evaluation.

The study conformed to the Declaration of Helsinki and was approved by the ethics committee of the Longhua hospital affiliated to Shanghai university of traditional Chinese medicine (approval number: 2020LCSY031). The study was registered on Chinese Clinical Trial Registry (ChiCTR) (Registration number: ChiCTR2100043369). All patients provided written informed consent prior to enrollment.

2.2. Diagnostic criteria for osteoporosis

Bone mineral density (BMD) measurements obtained with dual-energy X-ray bone absorptiometry (DXA) have been confirmed to be effective methods for diagnosing osteoporosis and assessing the risk of fragility fractures [12]. According to the T-score-based diagnosis of osteoporosis proposed in the Guidelines for Preclinical Assessment and Clinical Trials of Osteoporosis by the World Health Organization (WHO) [13], namely, compared with healthy adults of the same race and gender, the T-score ≥ -1 indicates normal bone mass; $-1 > T > -2.5$ indicates reduced bone mass; $T \leq -2.5$ indicates osteoporosis. All BMD measurements in this study were performed using a Dual-Energy X-ray Bone Densitometer (GE, USA).

2.3. Questionnaire survey

2.3.1. The physical examination information

Height, weight, body mass index (BMI), waist circumference, systolic blood pressure, and diastolic blood pressure. The basic information included educational level, marital status, and type of work mainly engaged (previously engaged). The special information on women included menopausal history, menopausal age, as well as gravidity and parity history.

2.3.2. The lifestyle habits

Dietary types, main foods consumed (rice, noodles, coarse grains, meat, vegetables, soy products, eggs, tea, coffee, carbonated drinks, and dairy products), daily sunshine time, weekly exercise forms, and weekly exercise frequency.

2.3.3. Medical history

Hypertension, hyperlipidemia, diabetes, stroke, coronary heart disease, fractures, family fractures, family hunchback, lumbar disc herniation, knee osteoarthritis, gout, hyperthyroidism, hypothyroidism, rheumatoid arthritis, systemic lupus erythematosus.

2.3.4. The health behavior information

Drinking, smoking, intake of dairy products, amount of exercise, intake of drugs (calcium, vitamin D3, antihypertensive drugs, hypoglycemic drugs, platelet aggregation inhibitors, lipid-lowering drugs, hormone drugs, traditional Chinese patent medicines and simple preparations).

2.3.5. TCM syndrome information

Fatigue and lack of strength, shortness of breath and unwillingness to speak, low and weak voice, eating less and having shapeless stools, dizziness or limb numbness, palpitations, insomnia, memory loss, chest tightness, or abdominal fullness, heavy head or body, sticky and greasy sensation in the mouth, phlegm and always feeling phlegm in the throat, sticky stools or feeling unable to fully defecate, irritability or unfounded sighs, fullness or distending pain in the chest and hypochondrium, dry and bitter mouth, constipation or dry stools, fever sensation in the urethra during urination, deep urine color, pain in a certain part of the body with localized pain (cone pain), dysphoria in chest, palms, and soles, large food intake with rapid hungering, dry mouth and throat, frequent nocturia, physical or local chilly sensation or cold limbs, lumbar debility, tinnitus or deafness, hair loss or tooth shaking, yellowish or pale complexion, facial blush on both cheekbones, flushed face and congested eyes, skin mucosal ecchymosis or abnormal veins, or rough, dry, and brown skin, pale lips and nails, cyanosis of the lips and nails, tongue texture, tongue coating, and pulse condition.

2.3.6. Other information

1. Have parents been diagnosed with osteoporosis or have they suffered fractures after a light fall? 2. Have you ever fallen (more than once last year), or are you worried about falling due to your weak body? 3. Has the height decreased by more than 3 cm after the age of 40? 4. Female questionnaire questions: Have you had your ovaries removed before the age of 50 without taking estrogen or progesterone supplements? 5. Male questionnaire questions: Have you ever experienced symptoms related to impotence, decreased libido, or other low androgen levels? 6. Do you exercise less than 30 min per day? 7. Have you ever been unable to consume dairy products without taking calcium tablets? 8. Have you been engaged in outdoor activities for less than 10 min every day without taking vitamin D? 9. Have you ever taken steroids for more than 3 consecutive months?

2.4. Statistical analysis

Data analysis was performed using the SPSS 24.0 statistical software. Continuous variables were expressed as mean ± standard deviation, and grouping variables were represented as number and constituent ratio (%), which were processed using independent sample *t*-test and chi-square test, respectively. Univariate analysis was implemented to find the influencing factors of osteoporosis. The multivariate logistic regression model was constructed based on the univariate analysis results, and osteoporosis risk prediction models were respectively constructed for females and males. The receiver operating characteristic (ROC) curves and Hosmer-Lemeshow goodness-of-fit test were used for the model evaluation [14].

3. Results

3.1. Basic characteristics of the study population

A total of 3000 subjects were enrolled in this study, including 2243 women (74.8 %). The mean age of both women and men was approximately 55 years old. The mean height and weight of men were about 169 cm and 68 kg, respectively, which were significantly higher than the mean height of women (160 cm) and the mean weight of women (60 kg). The mean systolic and diastolic blood

Table 1
Basic characteristics of the study population.

Variable	Female	Male	*P*-value
Case	2243	757	
Age (years)	54.94 (6.90)	55.18 (6.29)	0.404
Height (cm)	159.60 (5.49)	168.51 (7.18)	<0.001
Weight (kg)	60.61 (9.33)	68.16 (12.65)	<0.001
BMI (kg/m^2)	26.22 (6.40)	26.06 (7.04)	0.576
Waist (cm)	82.60 (164.87)	82.25 (8.99)	0.953
Systolic pressure (mmHg)	120.79 (12.49)	123.05 (13.17)	<0.001
Diastolic pressure (mmHg)	79.10 (8.01)	80.66 (9.28)	<0.001
BMD (g/cm^2)	−1.54 (1.34)	−1.55 (1.31)	0.868
T-value			0.416
$T \geq -1$, %	649 (28.9)	212 (28.0)	
$-1 > T > -2.5$, %	1102 (49.1)	392 (51.8)	
$T \leq -2.5$, %	492 (21.9)	153 (20.2)	

Table 2
Univariate analysis of the factors affecting osteoporosis in women.

Variable	Osteoporosis group (n = 492)		Non-osteoporosis group (n = 1751)		χ^2	*P*
	Case	Constituent ratio (%)	Case	Constituent ratio (%)		
Age (years)					40.232	< **0.001**
<50	60	12.2	454	25.9		
≥50	432	87.8	1297	74.1		
BMI (kg/m^2)					39.925	< **0.001**
<24	207	42.1	1020	58.3		
≥24.0	285	57.9	731	41.7		
Menopause					2.312	0.128
No	23	4.7	117	6.7		
Yes	469	95.3	1634	93.3		
Menopausal age (years)					0.754	0.385
<45	22	4.7	96	5.9		
≥45	447	95.3	1538	94.1		
Mainly engaged in physical labor					0.178	0.673
No	272	55.3	989	56.5		
Yes	220	44.7	762	43.5		
Less physical exercise					0.176	0.675
No	396	80.5	1392	79.5		
Yes	96	19.5	359	20.5		
Daily exposure to sunlight > 30 min					11.085	**0.001**
No	396	80.5	1392	79.5		
Yes	96	19.5	359	20.5		
No intake of dairy products					10.718	**0.001**
No	388	78.9	1491	85.2		
Yes	104	21.1	260	14.8		
Hypertension					0.256	0.613
No	408	82.9	1471	84.0		
Yes	84	17.1	280	16.0		
Hyperlipidemia					1.716	0.190
No	429	87.2	1483	84.7		
Yes	63	12.8	268	15.3		
Diabetes mellitus					0.281	0.596
No	442	89.8	1556	88.9		
Yes	50	10.2	195	11.1		
Coronary heart disease					17.541	< **0.001**
No	447	90.9	1677	95.8		
Yes	45	9.1	74	4.2		
History of fractures					0.958	0.328
No	478	97.2	1715	97.9		
Yes	14	2.8	36	2.1		
Family history of fractures					0.766	0.381
No	481	97.8	1723	98.4		
Yes	14	2.8	36	2.1		
Lumbar disc herniation					6.851	**0.009**
No	423	86.0	1580	90.2		
Yes	69	14.0	171	9.8		
Osteoarthritis					0.012	0.912
No	408	82.9	1458	83.3		
Yes	84	17.1	293	16.7		
Gout					0.005	0.942
No	485	98.6	1723	98.4		
Yes	7	1.4	28	1.6		
Hypoglycemic drugs					0.192	0.661
No	456	92.7	1635	93.4		
Yes	36	7.3	116	6.6		
Platelet aggregation inhibitors					0.048	0.827
No	479	97.4	1710	97.7		
Yes	13	2.6	41	2.3		
Lipid-lowering drugs					<0.001	1.000
No	475	96.5	1692	96.6		
Yes	17	3.5	59	3.4		
No intake of calcium tablets and vitamin D					31.998	< **0.001**
No	237	48.2	1094	62.5		
Yes	255	51.8	657	37.5		
Insomnia					4.293	**0.039**
No	151	30.7	453	25.9		
Yes	341	69.3	1297	74.1		
Memory loss					1.023	0.312

(*continued on next page*)

Table 2 (*continued*)

Variable	Osteoporosis group (n = 492)		Non-osteoporosis group (n = 1751)		χ^2	*P*
	Case	Constituent ratio (%)	Case	Constituent ratio (%)		
No	184	37.4	609	34.8		
Yes	308	62.6	1141	65.2		
Sticky and greasy sensation in the mouth					1.905	0.167
No	62	12.6	180	10.3		
Yes	430	87.4	1570	89.7		
Lumbar debility					19.334	< **0.001**
No	351	71.3	1057	60.4		
Yes	141	28.7	694	39.6		
Dysphoria in chest, palms, and soles					0.887	0.346
No	160	32.5	611	34.9		
Yes	332	67.5	1138	65.1		
Dry mouth and throat					23.579	0.459
No	185	37.6	693	39.6		
Yes	307	62.4	1058	60.4		
Loose teeth and hair loss					0.549	**0.001**
No	257	52.2	761	43.5		
Yes	235	47.8	990	56.5		
Yellow urine					11.580	0.451
No	88	17.9	342	19.5		
Yes	404	82.1	1409	80.5		
Thready and rapid pulse					40.723	< **0.001**
No	415	84.3	1638	93.5		
Yes	77	15.7	113	6.5		
Intolerance of cold and cold limbs					0.106	0.735
No	225	45.7	783	44.7		
Yes	267	54.3	967	55.3		
Frequent nocturia					0.147	0.701
No	169	34.3	583	33.3		
Yes	323	65.7	1168	66.7		
Pale tongue with whitish coating					3.026	0.082
No	343	69.7	1145	65.4		
Yes	149	30.3	606	34.6		
Sunken and slow pulse					50.169	< **0.001**
No	405	82.3	1628	93		
Yes	87	17.7	123	7		
Flushed face and congested eyes					28.659	< **0.001**
No	46	9.3	348	19.9		
Yes	446	90.7	1403	80.1		
Pale lips and nails					2.019	0.155
No	94	19.1	389	22.2		
Yes	398	80.9	1362	77.8		

pressure in men were significantly higher than those in women, but there was no significant statistical difference between the two groups in BMI and waist circumference. The mean BMD values for women and men were almost identical, at −1.54 and −1.55, respectively. Meanwhile, a total of 492 women suffered from osteoporosis and 153 men suffered from osteoporosis. The proportion of osteoporosis patients in women was higher than that in men (21.9 % vs 20.2 %) (Table 1).

3.2. Univariate analysis of the factors affecting osteoporosis

3.2.1. Univariate analysis of the factors affecting osteoporosis in women

Univariate analysis of the factors influencing osteoporosis in women is shown in Table 2. The findings demonstrated that age, BMI, daily exposure to sunlight >30 min, no intake of dairy products, combined coronary heart disease, combined lumbar disc herniation, no intake of calcium tablets and vitamin D, insomnia, lumbar debility, flushed face and congested eyes, loose teeth and hair loss, thready and rapid pulse, as well as sunken and slow pulse exhibited notable statistical differences in women between the osteoporosis group and the non-osteoporosis group (all $P < 0.05$; Table 2).

3.2.2. Univariate analysis of the factors affecting osteoporosis in men

Univariate analysis for the factors influencing osteoporosis in men revealed that daily exposure to sunlight >30 min, no intake of dairy products, no intake of calcium tablets and vitamin D, insomnia, sticky and greasy sensation in the mouth, and pale tongue with whitish coating presented notable statistical differences in men between the osteoporosis group and the non-osteoporosis group (all $P < 0.05$; Table 3).

Table 3
Univariate analysis of the factors affecting osteoporosis in men.

Variable	Osteoporosis group (n = 492)		Non-osteoporosis group (n = 1751)		χ^2	*P*
	Case	Constituent ratio (%)	Case	Constituent ratio (%)		
Age (years)					0.355	0.551
<50	28	18.3	96	15.9		
≥50	125	81.7	508	84.1		
BMI (kg/m^2)					2.026	0.155
<24	63	41.2	290	48.0		
≥24.0	90	58.8	314	52.0		
Mainly engaged in physical labor					0.035	0.852
No	85	55.6	328	54.3		
Yes	68	44.4	276	45.7		
Less physical exercise					0.821	0.365
No	131	85.6	496	82.1		
Yes	22	14.4	108	17.9		
Daily exposure to sunlight > 30 min					10.566	**0.001**
No	74	48.4	204	33.8		
Yes	79	51.6	400	66.2		
No intake of dairy products					7.865	**0.005**
No	111	72.5	501	82.9		
Yes	42	27.5	103	17.1		
Hypertension					0.049	0.824
No	121	79.1	485	80.3		
Yes	32	20.9	119	19.7		
Hyperlipidemia					0.110	0.741
No	129	84.3	500	82.8		
Yes	24	15.7	104	17.2		
Diabetes mellitus					0.779	0.377
No	129	84.3	500	82.8		
Yes	17	11.1	86	14.3		
Coronary heart disease					0.011	0.915
No	146	95.4	580	96.0		
Yes	7	4.6	24	4.0		
History of fractures					1.988	0.159
No	125	81.7	523	86.6		
Yes	28	18.3	81	13.4		
Family history of fractures					2.514	0.113
No	142	92.8	581	96.2		
Yes	11	7.2	23	3.8		
Lumbar disc herniation					1.314	0.252
No	128	83.7	529	87.6		
Yes	25	16.3	75	12.4		
Osteoarthritis					0.009	0.923
No	122	79.7	477	79.0		
Yes	31	20.3	127	21.0		
Gout					0.836	0.361
No	144	94.1	581	96.2		
Yes	9	5.9	23	3.8		
Hypoglycemic drugs					0.381	0.537
No	140	91.5	540	89.4		
Yes	13	8.5	64	10.6		
Lipid-lowering drugs					0.235	0.628
No	143	93.5	573	95		
Yes	10	6.5	31	5.1		
No intake of calcium tablets and vitamin D					32.046	< **0.001**
No	55	35.9	373	62		
Yes	98	64.1	231	38		
Insomnia					6.540	**0.011**
No	43	28.1	111	18.4		
Yes	110	71.9	493	81.6		
Memory loss					2.394	0.122
No	53	34.6	168	27.9		
Yes	100	65.4	435	72.1		
Sticky and greasy sensation in the mouth					7.446	**0.006**
No	27	17.6	57	9.5		
Yes	126	82.4	545	90.5		
Lumbar debility					2.817	0.093
No	96	62.7	424	70.2		
Yes	57	37.3	180	29.8		
Dysphoria in chest, palms, and soles					0	1.000

(*continued on next page*)

Table 3 (*continued*)

Variable	Osteoporosis group (n = 492)		Non-osteoporosis group (n = 1751)		χ^2	*P*
	Case	Constituent ratio (%)	Case	Constituent ratio (%)		
No	53	34.6	211	34.9		
Yes	100	65.4	393	65.1		
Dry mouth and throat					0.580	0.446
No	63	41.2	226	37.4		
Yes	90	58.8	378	62.6		
Loose teeth and hair loss					0.481	0.488
No	63	41.2	270	44.7		
Yes	90	58.8	334	55.3		
Yellow urine					0.099	0.753
No	32	20.9	117	19.4		
Yes	121	79.1	487	89.7		
Thready and rapid pulse					2.267	0.132
No	144	94.1	542	89.7		
Yes	9	5.9	62	10.3		
Intolerance of cold and cold limbs					2.026	0.155
No	58	37.9	270	44.7		
Yes	95	62.1	334	55.3		
Frequent nocturia					2.563	0.109
No	49	32	238	39.5		
Yes	104	68	365	60.5		
Pale tongue with whitish coating					5.454	**0.020**
No	117	76.5	400	66.2		
Yes	36	23.5	204	33.8		
Sunken and slow pulse					0.098	0.755
No	138	90.2	537	88.9		
Yes	15	9.8	67	11.1		
Flushed face and congested eyes					2.799	0.094
No	23	15	130	21.5		
Yes	130	85	474	78.5		
Pale lips and nails					3.748	0.053
No	38	24.8	106	17.5		
Yes	115	75.2	498	82.5		

3.3. Multivariate analysis for the factors influencing osteoporosis

3.3.1. Multivariate analysis for the factors influencing osteoporosis in women

A multivariate logistic regression model for female osteoporosis was constructed by screening the variables with statistical differences in the univariate analysis, as shown in Table 4. The corresponding results disclosed that the logistic prediction model for osteoporosis in women was Logit (P) = −2.946 + 0.960 (age ≥50 years old) + 0.633 (BMI ≥24 kg/m^2) - 0.545 (daily exposure to sunlight >30 min) + 0.519 (no intake of dairy products) + 0.827 (coronary heart disease) + 0.383 (lumbar disc herniation) + 0.654 (no intake of calcium tablets and vitamin D) - 0.509 (insomnia) + 0.580 (flushed face and congested eyes) + 1.194 (thready and rapid pulse) + 1.309 (sunken and slow pulse).

3.3.2. Multivariate analysis for the factors impacting osteoporosis in men

A multivariate logistic regression model for male osteoporosis was screened for variables with statistical differences in the

Table 4
Multifactorial logistic regression analysis of female osteoporosis.

Variable		Control group	B	P	OR	95 % CI
Age (years)	≥50	<50	0.960	< **0.001**	2.612	1.934–3.583
BMI (kg/m^2)	≥24	<24	0.633	< **0.001**	1.883	1.507–2.355
Daily exposure to sunlight > 30 min	Yes	No	−0.545	< **0.001**	0.580	0.465–0.723
No intake of dairy products	Yes	No	0.519	< **0.001**	1.680	1.262–2.227
Coronary heart disease	Yes	No	0.827	< **0.001**	2.286	1.481–3.497
Lumbar disc herniation	Yes	No	0.383	**0.025**	1.467	1.045–2.043
No intake of calcium tablets and vitamin D	Yes	No	0.654	< **0.001**	1.924	1.546–2.397
Insomnia	Yes	No	−0.509	< **0.001**	0.601	0.463–0.782
Lumbar debility	Yes	No	−0.189	0.147	0.828	0.640–1.068
Flushed face and congested eyes	Yes	No	0.580	**0.001**	1.785	1.259–2.578
Loose teeth and hair loss	Yes	No	0.024	0.842	1.024	0.814–1.290
Thready and rapid pulse	Yes	No	1.194	< **0.001**	3.301	2.265–4.808
Sunken and slow pulse	Yes	No	1.309	< **0.001**	3.703	2.548–5.386
Constant	–	–	−2.946	< **0.001**	0.053	0.031–0.0889

univariate analysis, and the results in Table 5 unveiled that the logistic prediction model for osteoporosis in men was Logit (P) = −1.152–0.644 (daily exposure to sunlight >30 min) + 0.975 (no intake of calcium tablets and vitamin D) - 0.488 (insomnia).

3.4. Model evaluation

3.4.1. Evaluation of the diagnostic efficacy of the osteoporosis prediction model

As shown in Fig. 1, the area under the ROC curve (ROC-AUC) of the female and male osteoporosis prediction models was 0.743 (Fig. 1-A) and 0.679 (Fig. 1-B), respectively. The AUC in both groups was greater than 0.5, implying that the prediction model for osteoporosis risk in women and men had better diagnostic performance.

3.4.2. Goodness-of-fit evaluation of the osteoporosis prediction model

The goodness-of-fit of the female and male osteoporosis risk prediction models was tested based on the Hosmer-Lemeshow goodness-of-fit test. The goodness-of-fit results of the female osteoporosis prediction model ($\chi^2 = 10.270$, $P = 0.247$) and the male osteoporosis prediction model ($\chi^2 = 6.982$, $P = 0.539$) coincided with the actual situation.

4. Discussion

Osteoporosis is a serious public health problem, and its incidence is rising with an increase in life expectancy and lifestyle changes such as altered dietary intake and reduced physical activity [4]. This multicenter study have explored the factors influencing osteoporosis in women and men and constructed the osteoporosis risk prediction models that integrate traditional clinical information and TCM syndrome. We have found that there were significant differences in the factors influencing osteoporosis between women and men. TCM syndromes were associated with the risk of osteoporosis, and TCM syndrome information may be used for predicting the occurrence of osteoporosis.

A study published in 2009 found that the prevalence of osteoporosis in the Chinese mainland was about 13 % by investigating relevant studies published between 1980 and May 2008 [4]. Another study in 2019 suggested that the overall prevalence of osteoporosis in men was 10–20 % in China [5]. A total of 3000 adults aged 30–82 years were enrolled in this study. Of these, 2243 were female, accounting for about 75 % of the total study population, and 757 were male, accounting for 25 % of the total study population. Similar to the findings of the aforementioned study, our research has discovered the overall incidence of osteoporosis in the population was 21.5 %, and the proportion of osteoporosis patients in women was slightly higher than that in men (21.9 % vs 20.2 %). This result is also consistent with traditional epidemiological concepts that osteoporosis mainly occurs in postmenopausal and premenopausal women, as well as older men aged >50 years [15].

Osteoporosis can be caused by various factors, including age, genetic factors, hormone therapy, and prolonged bed rest [16,17]. The variables affecting osteoporosis in this study included multi-dimensional information such as traditional clinical demography information, physical examination information, female information, living habits, past medical history, other information, TCM syndrome information. Based on gender grouping, we explored the risk factors related to osteoporosis for men and women respectively. The results of this study found that the non-TCM syndrome information related to female osteoporosis included age, BMI, daily exposure to sunlight >30 min, no intake of dairy products, concomitant coronary heart disease, concomitant lumbar disc herniation, no intake of calcium tablets and vitamin D, and insomnia, while the TCM syndrome-related factors were lumbar debility, flushed face and congested eyes, loose teeth and hair loss, thready and rapid pulse, and sunken and slow pulse. The non-TCM syndrome information related to male osteoporosis included daily exposure to sunlight >30 min, no intake of dairy products, no intake of calcium tablets and vitamin D supplements, and insomnia, while the TCM syndrome-related factors were sticky and greasy sensation in the mouth and pale tongue with whitish coating.

The *Art of Health Cultivation in Ancient Times of the Yellow Emperor's Classic of Medicine* recorded that "a girl in 7 years old had a vigorous kidney qi, her deciduous teeth were changed and her hair began to flourish … …when a woman was 28 years old, her muscles and bones were strong, and her hair growth reached the most vigorous stage, at which time her body was the strongest … …when a woman was 49 years old, the Qi and blood of the Ren channel and Taichong were weakened, and she came to menopause with aging body and loss of fertility.". The rise and fall of kidney essence is closely associated with the tenacity of women. As women age, the secretion of estrogen decreases after menopause, which is consistent with the changes produced by the "depletion of Tiankui" in Chinese medicine. The gain and loss of Tiankui are tightly related to kidney essence. Therefore, deficiency of kidney essence, deficiency of Chong channel and Ren channel, desiccated bone, and reduced marrow, and lack of nourishment of the bone are the causes of

Table 5
Multifactorial logistic regression analysis of male osteoporosis.

Variable		Control group	B	P	OR	95 % CI
Daily exposure to sunlight > 30 min	Yes	No	−0.644	< **0.001**	0.525	0.359–0.768
No intake of dairy products	Yes	No	0.365	0.107	1.440	0.918–2.232
No intake of calcium tablets and vitamin D	Yes	No	0.975	< **0.001**	2.652	1.812–3.912
Insomnia	Yes	No	−0.488	**0.035**	0.614	0.392–0.973
Sticky and greasy sensation in the mouth	Yes	No	0.543	0.054	1.722	0.980–2.974
Pale tongue with whitish coating	Yes	No	−0.397	0.068	0.672	0.434–1.022
Constant	–	–	−1.152	< **0.001**	0.316	0.185–0.527

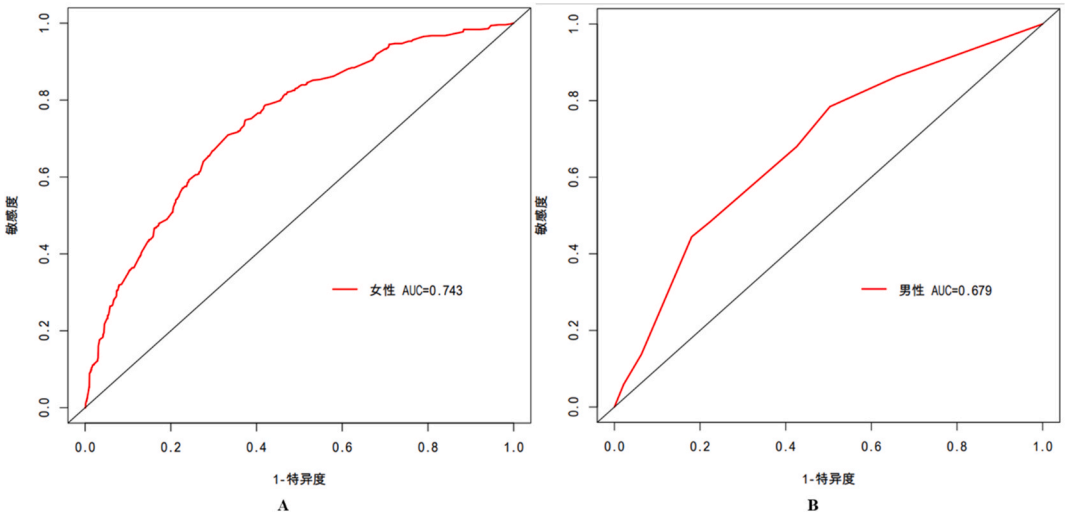

Fig. 1. ROC curved of osteoporosis risk prediction model for women and men.

joint lesions. Therefore, combined with the results of this study, it is found that kidney essence deficiency is the main pathogenesis of osteoporosis in women. The rise and fall of kidney essence directly determine the strength and weakness of bone growth and development: if the kidney essence is sufficient, the bone marrow is biochemically, and the bone is powerful; deficiency of kidney essence will lead to a biochemical deficiency of bone marrow, bone loss, and bone weakness, leading to osteoporosis.

Previous studies have demonstrated that a healthy diet and lifestyle can significantly reduce the occurrence of osteoporosis [18] and hinder disease progression in the early stages, leading to the most cost-effective disease treatment [19]. Some scholars formulated an early risk prediction tool for osteoporotic fractures based on demographic characteristics and TCM symptoms in women aged 40–65 years [20] and screened the TCM syndrome deficiency of liver-yin and kidney-yin, including restless fever of hands and feet, night sweats, debility of the legs, dizziness, blurred vision, dry and astringent eyes, aversion to heat, alopecia, luxated teeth, bitter taste, irritability, afternoon tidal fever, insomnia, dreaminess and easy to awake, fullness and discomfort in chest and hypochondrium, and lower limb cramps. Although the TCM syndrome information considered in the above-mentioned study has no similarities with our study, both studies demonstrate the potential value of TCM syndrome information in constructing a risk prediction model for osteoporosis.

Finally, this study constructed risk prediction models for osteoporosis in women and men based on the multifactorial logistic regression analysis, and the AUC reached 0.743 and 0.679, respectively, suggesting the favorable diagnostic efficacy. In addition, the goodness-of-fit of the osteoporosis prediction model also exceeded 0.05 in women and men, demonstrating that the prevalence of osteoporosis predicted by the model was in good agreement with the actual prevalence. However, The participants were mainly from the northernmost and easternmost regions of China, which may limit the generalizability of our findings. Similar studies be conducted in other regions of China or even in other countries to validate our results and gain a more comprehensive understanding of the impact of living environments on osteoporosis. What's more, it is important to note that the feasibility of integrating TCM syndromes into routine clinical settings for osteoporosis risk assessment may vary depending on factors such as healthcare infrastructure, availability of TCM practitioners, and cultural acceptance. Further research and practical implementation studies are needed to evaluate the benefits, challenges, and feasibility of such integration.

5. Limitation

There are obvious shortcomings in this study. At first, the age of the study population is limited to 30–82 years old, and the applicability of the model to patients in other age groups needs to be further explored. Secondly, the proportion of females is relatively high, while the number of males is relatively small. Thirdly, the information is mostly collected using questionnaires, which require independent recall of the research subjects and may have memory bias and affect the correctness of data collection. Fourth, the use of logistic regression modeling cannot handle the potential interaction between non-linear relationship ensemble variables. Lastly, the results have not been validated on an external dataset to assess the model's generalizability.

6. Conclusion

In summary, osteoporosis is more prevalent in women than in men, and significant differences exist in the risk factors affecting osteoporosis between the two genders. TCM syndromes have been found to be associated with the risk of osteoporosis. The constructed osteoporosis risk prediction model, incorporating conventional clinical information and TCM evidence, demonstrates good diagnostic efficacy and goodness-of-fit for both women and men. Further clinical application can be explored to provide evidence-based medical

evidence for early diagnosis and intervention of osteoporosis.

Funding

This study was funded by the National key Research and Development Program (No: 2019YFC1709905); Shanghai Three-year Action Plan to Further Accelerate the Inheritance and Innovation of TCM (ZY(2021–2023)-0201-01); Pudong Health System Pudong Famous Traditional Chinese Medicine Training Program (PWRzm2020-15); Shanghai University of Traditional Chinese Medicine 2022 Emergency Scientific Research Project on Omicron Infection with Novel Coronavirus Pneumonia (2022YJ-48); Xuhui District Artificial Intelligence Medical Hospital Cooperation Project (2021–016).

Ethics statement

This study was designed in accordance with the Declaration of Helsinki and approved by the ethics committee of Longhua hospital affiliated to Shanghai university of traditional Chinese medicine (approval number: 2020LCSY031). Informed consent was obtained from all participants involved in the study.

Data availability

Data will be made available on request.

CRediT authorship contribution statement

Dan Liu: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Zhijun Hu:** Conceptualization, Data curation, Writing – review & editing. **Zhanying Tang:** Formal analysis, Methodology, Writing – review & editing. **Pan Li:** Data curation, Supervision, Writing – review & editing. **Weina Yuan:** Formal analysis, Investigation, Supervision, Writing – review & editing. **Fangfang Li:** Formal analysis, Validation, Writing – review & editing. **Qian Chen:** Data curation, Methodology, Writing – review & editing. **Wen Min:** Supervision, Validation, Writing – review & editing. **Changwei Zhao:** Methodology, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to acknowledge the reviewers for their helpful comments on this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21501.

List of abbreviation

IOF	International Osteoporosis Foundation
TCM	traditional Chinese medicine
BMD	Bone mineral density
DXA	dual-energy X-ray bone absorptiometry
WHO	World Health Organization
ROC	receiver operating characteristic

References

[1] A.K. Anam, K. Insogna, Update on osteoporosis screening and management, Med Clin North Am 105 (2021) 1117–1134, https://doi.org/10.1016/j.mcna.2021.05.016.

[2] G. Rinonapoli, C. Ruggiero, L. Meccariello, M. Bisaccia, P. Ceccarini, A. Caraffa, Osteoporosis in men: a review of an underestimated bone condition, Int. J. Mol. Sci. 22 (2021), https://doi.org/10.3390/ijms22042105.

[3] J.M. Kling, B.L. Clarke, N.P. Sandhu, Osteoporosis prevention, screening, and treatment: a review, J Womens Health (Larchmt) 23 (2014) 563–572, https://doi.org/10.1089/jwh.2013.4611.

[4] A. Aibar-Almazán, A. Voltes-Martínez, Y. Castellote-Caballero, D.F. Afanador-Restrepo, M.D.C. Carcelén-Fraile, E. López-Ruiz, Current status of the diagnosis and management of osteoporosis, Int. J. Mol. Sci. 23 (2022), https://doi.org/10.3390/ijms23169465.
[5] F. Yu, W. Xia, The epidemiology of osteoporosis, associated fragility fractures, and management gap in China, Arch. Osteoporosis 14 (2019) 32, https://doi.org/10.1007/s11657-018-0549-y.
[6] L. Cianferotti, C. Cricelli, J.A. Kanis, R. Nuti, J.Y. Reginster, J.D. Ringe, et al., The clinical use of vitamin D metabolites and their potential developments: a position statement from the European society for clinical and economic aspects of osteoporosis and osteoarthritis (ESCEO) and the international osteoporosis foundation (IOF), Endocrine 50 (2015) 12–26, https://doi.org/10.1007/s12020-015-0606-x.
[7] P. Proia, A. Amato, P. Drid, D. Korovljev, S. Vasto, S. Baldassano, The impact of diet and physical activity on bone health in children and adolescents, Front. Endocrinol. 12 (2021), 704647, https://doi.org/10.3389/fendo.2021.704647.
[8] J. Smets, E. Shevroja, T. Hugle, W.D. Leslie, D. Hans, Machine learning solutions for osteoporosis-A review, J. Bone Miner. Res. 36 (2021) 833–851, https://doi.org/10.1002/jbmr.4292.
[9] T.J. Aspray, T.R. Hill, Osteoporosis and the ageing skeleton, Subcell. Biochem. 91 (2019) 453–476, https://doi.org/10.1007/978-981-13-3681-2_16.
[10] W. Liu, L.H. Yang, X.C. Kong, L.K. An, R. Wang, Meta-analysis of osteoporosis: fracture risks, medication and treatment, Minerva Med. 106 (2015) 203–214.
[11] The Development Plan of TCM Health Services, (2015-2020) issued by the general office of the State Council, Chinese Medical Culture 10 (2015) 26.
[12] K.N. Haseltine, T. Chukir, P.J. Smith, J.T. Jacob, J.P. Bilezikian, A. Farooki, Bone mineral density: clinical relevance and quantitative assessment, J. Nucl. Med. 62 (2021) 446–454, https://doi.org/10.2967/jnumed.120.256180.
[13] J.A. Kanis, Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group, Osteoporos. Int. 4 (1994) 368–381, https://doi.org/10.1007/BF01622200.
[14] M.W. Fagerland, D.W. Hosmer, A goodness-of-fit test for the proportional odds regression model, Stat. Med. 32 (2013) 2235–2249, https://doi.org/10.1002/sim.5645.
[15] W. Liu, L.H. Yang, X.C. Kong, et al., Meta-analysis of osteoporosis: fracture risks, medication and treatment, Minerva Med. 106 (2015) 203–214.
[16] T.A. Azeez, Osteoporosis and cardiovascular disease: a review, Mol. Biol. Rep. 50 (2023) 1753–1763, https://doi.org/10.1007/s11033-022-08088-4.
[17] S. Khandelwal, N.E. Lane, Osteoporosis: review of etiology, mechanisms, and approach to management in the aging population, Endocrinol Metab. Clin. N. Am. 52 (2023) 259–275, https://doi.org/10.1016/j.ecl.2022.10.009.
[18] S.K. Papadopoulou, K. Papadimitriou, G. Voulgaridou, E. Georgaki, E. Tsotidou, O. Zantidou, et al., Exercise and nutrition impact on osteoporosis and sarcopenia-the incidence of osteosarcopenia: a narrative review, Nutrients 13 (2021), https://doi.org/10.3390/nu13124499.
[19] Y. Wan, F. Zeng, H. Tan, Y. Lu, Y. Zhang, L. Zhao, et al., Cost-effectiveness analyses of denosumab for osteoporosis: a systematic review, Osteoporos. Int. 33 (2022) 979–1015, https://doi.org/10.1007/s00198-021-06268-9.
[20] Y.W. Lan Ch, Construction of a risk assessment model for osteoporosis, Journal of Guangxi Sciences 27 (2020) 676–685.