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Application of neural network and nomogram for the prediction of risk factors for bone mineral density abnormalities: A cross-sectional NHANES-based survey

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ABSTRACT

Background: The risk of bone mineral density abnormalities is inconsistent between eastern and western regions owing to differences in ethnicity and dietary habits. A diet comprising carbohydrates and dietary fiber is not the common daily diet of the American population. Thus far, no studies have assessed the risk of bone mineral density abnormalities in the American population, and no predictive model has considered the intake of carbohydrates, dietary fiber, and coffee, as well as levels of various electrolytes for assessing bone mineral density abnormalities, especially in the elderly. This study conducted a neural network analysis and established a predictive nomogram considering an unusual diet to determine risk factors for bone mineral density abnormalities in the American population, mainly to provide a reference for the prevention and treatment of related bone mineral density abnormalities.

Methods: Overall, 9871 patients who had complete data were selected from the National Health and Nutrition Examination Survey database during 2017–2020 as the research object, and patients' general clinical characteristics were compared. Neural networks and nomograms were analyzed to screen for and quantify risk factors for bone mineral density abnormalities. Finally, the receiver operating characteristic (ROC) curve, calibration curve, decision curve analysis (DCA), and community indifference curve (CIC) were constructed to comprehensively verify the accuracy, differential ability, and clinical practicability of the neural network and nomogram.

Results: The important risk factors for bone mineral density abnormalities were caffeine intake, carbohydrate consumption, body mass index (BMI), height, blood sodium, blood calcium, blood phosphorus, blood potassium, dietary fiber, vitamin D, participant age, weight, race, family history, and sex. The nomogram revealed that caffeine intake, carbohydrate consumption, blood potassium, and age were positively correlated with bone mineral density abnormalities, whereas BMI, height, blood phosphate, dietary fiber, and blood sodium were negatively correlated with bone mineral density abnormalities. Women were more prone to these abnormalities than men. The area under the ROC curve values of the neural network and nomogram were 85.8 % and 77.7 %, respectively. The Youden index was 58.04 % and 41.87 %, respectively. The detection

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sensitivity was 75.73 % and 65.06 %, respectively, and the specificity was 82.31 % and 76.81 %, respectively. Calibration curves of the neural network and nomogram showed better discrimination ability from the standard curve ($P > 0.05$). DCA and CIC analyses showed that the application of the neural network and nomogram to explore risk factors for bone mineral density abnormalities had certain clinical practicability, and the overall predictive effect of the model was good.

Conclusion: The outcomes of the neural network and nomogram analyses suggested that diet structure and electrolyte changes are important significant risk factors for bone mineral density abnormalities, especially with increasing carbohydrate and caffeine intake and decreasing dietary fiber intake. The established model can also provide a reference for future risk prediction.

1. Introduction

bone mineral density abnormalities, including osteoporosis and osteopenia, represent a disease of osteopenia and/or associated bone destruction involving an abnormal primary bone mineral density in the elderly and postmenopausal women and an abnormal idiopathic bone mineral density. With the aging of the population, the number of people with bone mineral density abnormalities is increasing [1]. According to literature reports [2],the prevalence of femoral neck BMD T score ≤ -2.5 among people aged 50 and above in the UK is 6.8 % for males and 21.8 % for females.The total direct costs in 2019 were £ 5.4 billion.In addition, approximately 54 million people in the United States suffer from osteoporosis or low bone mineral density in the femoral neck and lumbar spine [3]. Therefore, assessing the risk factors and reducing risks have become important to alleviate osteoporosis and osteopenia, as well as the resulting fractures and deaths, and to reduce public and private burden [4]. These abnormalities are usually asymptomatic in the early stage and cannot be detected until the affected person has a history of trauma such as fracture, which delays both diagnosis and treatment and increases the burden [5]. In addition to traditional risk factors such as older age, estrogen, vitamin D, and hormone use, among others [6], dietary structure and electrolyte disorders may also be important risk factors for the onset of an abnormal primary bone mineral density, especially based on the dietary structure of the American population [7]. Moreover, several algorithm models [8] have been widely used in the prevention and treatment of bone mineral density abnormalities, for example, Neural network analysis [9,10] can reveal important risk factors related to bone mineral density abnormalities. It simulates the neural network system of the human brain for structural operation, and information processing is achieved by adjusting the network of several internal nodes. But the widely used algorithm currently includes alcohol drinking, age, smoking, parents' fracture history, height difference ($\geq$4 cm), use of glucocorticoids and other drugs, endocrine diseases, milk, premature menopause history, gender, fracture history, body mass index (BMI), and other conventional risk factors in the study [11]. Thus far, no model has considered carbohydrates, dietary fibers, coffee consumption, and electrolytes in relevant modeling studies on the American population, and previous studies have mostly focused on bone mineral density differences in postmenopausal women; only a few studies have assessed bone mineral density abnormalities in the elderly. Therefore, the present study conducted a neural network analysis and established a risk prediction model (a predictive nomogram) considering the unusual diet structure of the American population, and we used relevant physical examination indexes such as electrolytes and other parameters to generate a tool for the prevention of bone mineral density abnormalities in this relevant population.

2. Materials and methods

2.1. Data and research population

This study used data from the National Health and Nutrition Examination Survey (NHANES) database by logging into the official website of the NHANES, followed by downloading and sorting the NHANES data for the period 2017–2020. The NHANES is a multilevel and widely representative public database, and it is continuously updated; that is, it extensively collects data from the American population every year. All participants signed the informed consent form of the NHANES.

The latest NHANES data for the period 2017–2020 were selected, and a total of 9871 patients who had complete data on bone mineral density (BMD) of the femoral neck and sex, age, race, family history of parents' fractures, height, weight, carbohydrates, dietary fiber, coffee, and vitamin D,blood phosphorus, blood potassium, blood sodium, blood calcium were selected. Overall, the study population included 5362 male and 4509 female patients, with an age range of 50–80 years.

2.2. Research variables

In this study, patients with a T value of <-1 calculated according to the femoral neck BMD were included in the abnormal bone mineral density group, as the study outcome variable. Independent variables were sex, age, race, family history of parents' fractures, height, weight, BMI, and other general conventional indexes calculated from the patients. Additionally, unusual dietary structures of the American population, such as intake of carbohydrates, dietary fiber, coffee, and vitamin D, as well as levels of electrolytes such as blood phosphorus, blood potassium, blood sodium, and blood calcium, which may be caused by dietary disorders, were included.

2.3. Statistical analysis

SPSS 26.0, R software 4.0.3 (64-bit), MedCalc19.0.4 and python3.11.4were used for the statistical analysis of data. Measurement data were expressed as ($\overline{x} \pm s$) or median (quartile). Counting data are expressed as a rate or constituent ratio. Data on general clinical characteristics were compared between the abnormal bone mineral density group (case group) and the normal bone mineral density group (control group). The measurement data conforming to the normal distribution were statistically analyzed using the independent-sample *t*-test, and measurement data not conforming to the normal distribution were statistically analyzed using a nonparametric test. Counting data were analyzed using the chi-square test. We first trained the Multilayer Perceptron(MLP) neural network to identify important risk factors, screened the risk factors that had significance using logistic univariate and multivariate regression models, and assigned the risk score to variables that were significant as screened with the logistic regression model using a nomogram. Finally, we applied the receiver operating characteristic (ROC) curve, calibration curve (calibration), and decision curve analysis (DCA), and clinical impact curve (CIC) to comprehensively evaluate the accuracy, discrimination ability, and clinical practicability of the neural network and nomogram. The rms package was used to analyze the nomogram and calibration curve, and the rmda package was used to analyze DCA and CIC results. This study used K-fold cross validation to perform internal validation on the neural network, with a setting of 10 fold,

Need to use cross in Python_ Val_ Score, kFold mode.$P < 0.05$ indicated statistical significance.

3. Results

3.1. General characteristics of the study patients

After excluding participants with missing data of outcome variables and independent variables, a total of 9871 patients were included in the study population, 4103 cases of abnormal bone mineral density (case group) and 5768 subjects with normal bone mineral density (control group). Compared with the control group, the case group had an increase in age, carbohydrate, coffee, blood phosphorus, and blood potassium ($P < 0.05$) but a decrease in vitamin D,height, weight, BMI, dietary fiber, and blood sodium ($P < 0.05$); female sex, family history of fracture, and parents' race were associated with bone mineral density abnormality ($P < 0.05$; Table 1 and Fig. 1).

3.2. Training the neural network to determine the importance of risk factors

The input layer included all independent variables, and the output layer included the outcome variable. The training data were analyzed using the neural network. The results revealed that the important independent variables were coffee intake, carbohydrate consumption, BMI, height, blood sodium, blood calcium, blood phosphorus, blood potassium, dietary fiber, vitamin D use, age, weight, race, family history of fractures, and sex. The true-positive rate of the model after training was 70 %, and the true-negative rate was 82 % (Fig. 2).

3.3. Risk factor quantification by scoring in a nomogram based on logistic regression

Univariate and multivariate logistic regression analyses revealed that coffee intake, carbohydrate consumption, blood potassium, and age were positively correlated with bone mineral density abnormalities ($P < 0.05$), whereas BMI, height, blood phosphate, dietary fiber, and blood sodium were negatively correlated with bone mineral density abnormalities ($P < 0.05$). Additionally, females were more prone to abnormalities in bone mineral density than males ($P < 0.05$). The nomogram was used to score the 10 risk factors

Table 1
Comparison of clinical data between the case group and the control group with bone mineral density abnormalities.

variable	case group	control group	*t/z value*	*P* value
Number of cases	4103	5768	–	–
Gender(male)	1592(38.80 %)	3770(65.36 %)	681.597	0.000
Age(years)	68.36 ± 8.86	64.64 ± 8.62	20.895	0.000
Weight(Kg)	75.10 ± 16.95	90.51 ± 20.06	−40.051	0.000
Height(cm)	162.93 ± 9.28	169.01 ± 9.49	−31.662	0.000
BMI(kg/m^2)	28.24 ± 5.72	31.65 ± 6.43	−27.172	0.003
Family history(positive)	678(16.52 %)	764(13.24 %)	31.864	0.000
Race(Other races)	502(12.23 %)	639(11.07 %)	556.596	0.000
Carbohydrate(g)	201(132)	215(129)	3.505	0.000
Dietary fiber(g)	15.20 ± 9.84	15.99 ± 9.73	−3.972	0.000
Vitamin D(mg)	3.1(4.6)	3.4(4.4)	2.040	0.000
Caffeine(mg)	130(180)	104(199)	6.653	0.000
Blood phosphorus(mmlo/L)	1.16 ± 0.16	1.14 ± 0.17	4.127	0.000
Blood potassium(mmlo/L)	4.15 ± 0.41	4.13 ± 0.41	2.472	0.013
Blood calcium(mmlo/L)	9.31 ± 0.42	9.31 ± 0.39	−0.084	0.932
Blood sodium(mmlo/L)	140.51 ± 3.36	140.64 ± 2.72	−2.132	0.033

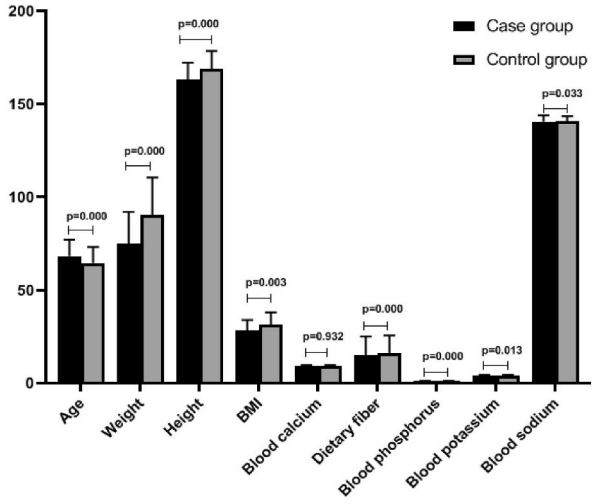

Fig. 1. Comparison of the distribution of continuous variables between the case group and the control group.

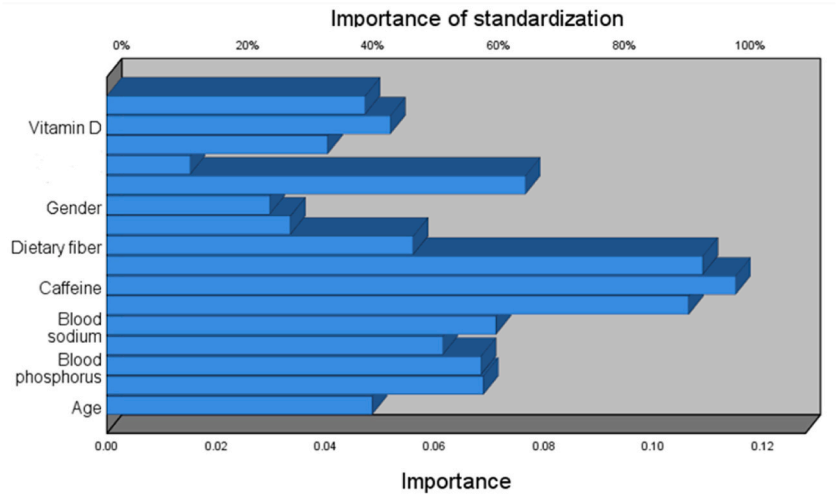

Fig. 2. Distribution of the important independent variables under neural network training for patients with bone mineral density abnormalities.

screened in logistic regression analysis. As for the highest scores, the patient age of 80 years was given a score of 28 points; additionally, the female sex, 18 points; daily coffee intake (3500 mg), 92 points; daily intake of dietary fiber (0 g), 25 points; daily intake of carbohydrates (1600 g), 47 points; the patient height of 135 cm, 57 points; BMI of 15 kg/m^2, 100 points; blood phosphate concentration of 0.6 mmol/L, 30 points; blood potassium concentration of 7.5 mmol/L, 21 points; and the blood sodium concentration of 120 mmol/L, 15 points. The prediction probability corresponding to each score was 0.054, and the score corresponding to each 1 % prediction probability was 18.333. When the total score was 240, the prediction probability reached 90 % (Table 2 and Fig. 3).

3.4. ROC curve, calibration curve, DCA, and CIC analyses to verify the accuracy, discrimination ability, and clinical practicability of the neural network and nomogram

The ROC curve, calibration curve (calibration), DCA, and CIC were established, wherein bone mineral density abnormality was the dependent variable, and the prediction probability obtained from the neural network and nomogram was the independent variable. The neural network and nomogram showed the following corresponding values: area under the ROC curve (AUC), 85.8 % and 77.7 %; Youden index, 58.04 %, and 41.87 %; sensitivity was 75.73 % and 65.06 %; and specificity, 82.31 % and 76.81 %. The calibration curve of the neural network and nomogram indicated that the prediction model had no significant difference when compared with the standard model ($P > 0.05$), and the discrimination ability of the model was good. DCA results showed that when the prediction probability of the nomogram reached 80 %, no clinical benefit was observed. When the prediction probability of the neural network reached 90 %, the net benefit rate was zero. CIC results further showed that the application of the neural network and nomogram in

Table 2
Results of univariate and multivariate logistic regression analyses of patients with bone mineral density abnormalities.

		Single-factor analysis	*P* value	Multi-factor analysis	*P* value
		OR value(95%*CI*)		*OR* value(95%*CI*)	
Female	–	1		1	
	+	2.976(2.739–3.233)	0.000	2.723(2.389–3.103)	0.000
Age	–	1		1	
	+	1.049(1.044–1.054)	0.000	1.051(1.045–1.057)	0.000
Weight	–	1	0.000	1	0.144
	+	0.953(0.950–0.955)		1.020(0.992–1.049)	
Height	–	1	0.000	1	0.000
	+	0.933(0.929–0.938)		0.933(0.908–0.960)	
BMI	–	1	0.000	1	0.000
	+	0.907(0.900–0.914)		0.848(0.786–0.914)	
Family history	–	1	0.000	1	0.728
	+	1.011(0.988–1.034)		0.995(0.969–1.021)	
Blood phosphorus	–	1	0.000	1	0.000
	+	1.631(1.292–2.059)		0.525(0.396–0.697)	
Blood potassium	–	1	0.013	1	0.000
	+	1.128(1.025–1.242)		1.264(1.128–1.418)	
Blood sodium	–	1	0.033	1	0.002
	+	0.985(0.972–0.998)		0.976(0.962–0.991)	
Carbohydrate	–	1	0.002	1	0.000
	+	0.999(0.999–0.999)		1.001(1.001–1.001)	
Dietary fiber	–	1	0.000	1	0.000
	+	0.991(0.987–0.995)		0.986(0.980–0.992)	
Caffeine	–	1	0.000	1	0.000
	+	1.001(1.001–1.001)		1.001(1.001–1.001)	

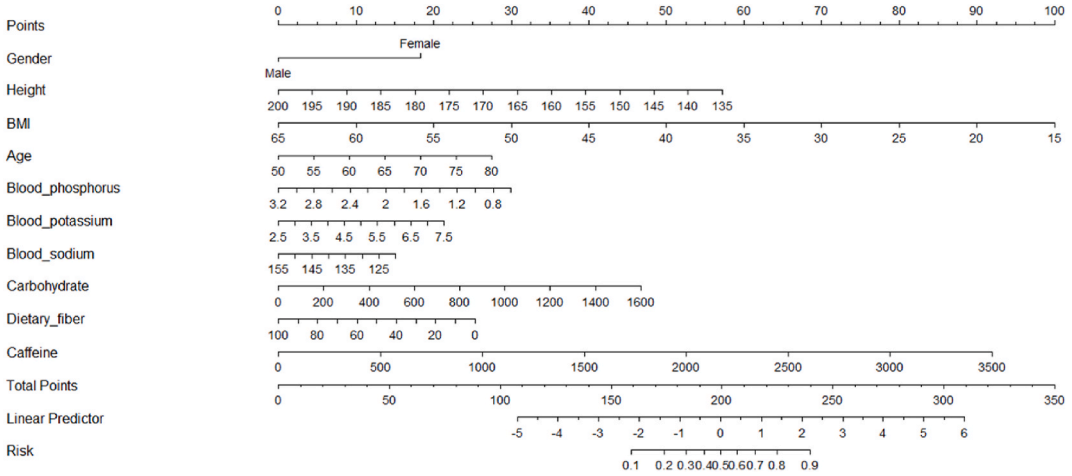

Fig. 3. Nomogram analysis of risk factors for bone mineral density abnormalities.

determining bone mineral density abnormalities has certain clinical practicability, and the overall prediction effect of the model was good (Figs. 4–6).

3.5. Internal validation of neural networks using 10 fold cross validation

This study used K-fold cross validation to perform internal validation on neural network, with a set of 10 folds. The results showed that the accuracy rates of the 10 cross validations were 0.706, 0.760, 0.762, 0.749, 0.771, 0.812, 0.714, 0.828, 0.750, 0.766.Average accuracy (K-fold cross validation) was 0.762.It indicates that the neural network model has good accuracy (Fig. 7).

4. Discussion

Osteoporosis and osteopenia are common metabolic diseases characterized by a low bone mineral density and micro-level degradation of the bone tissue. Currently, these conditions have become a global public health problem [12] and are closely related to age growth. With the continuous aging of the global population, osteoporosis and osteopenia have gradually become

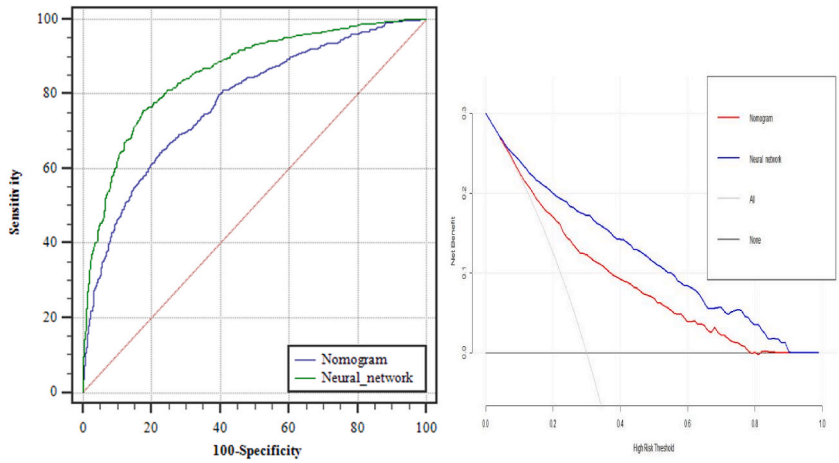

Fig. 4. (a) Receiver operating characteristic curve of neural network and nomogram. (b) Decision curve analysis of neural network and nomogram.

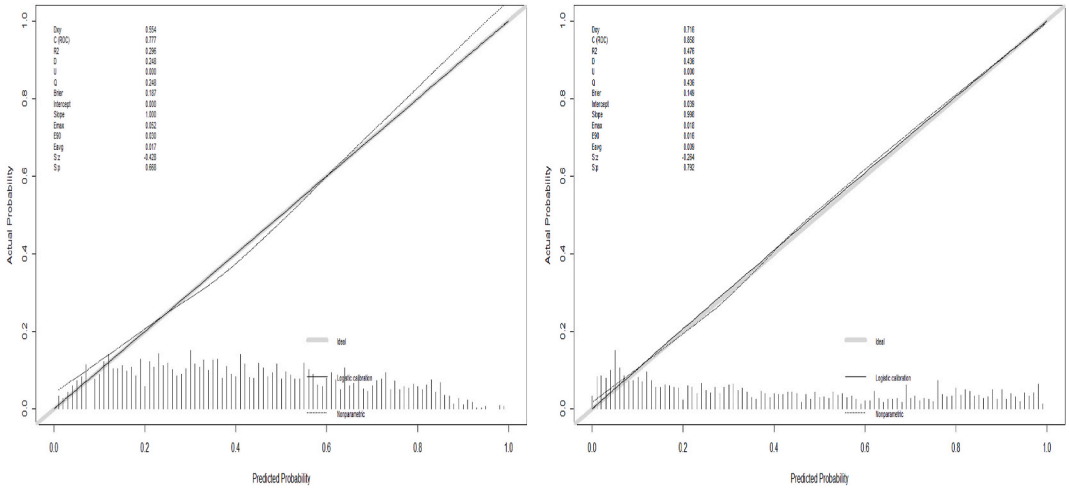

Fig. 5. (a) Calibration curve of neural network and nomogram.(b) Calibration curve of neural network and nomogram.

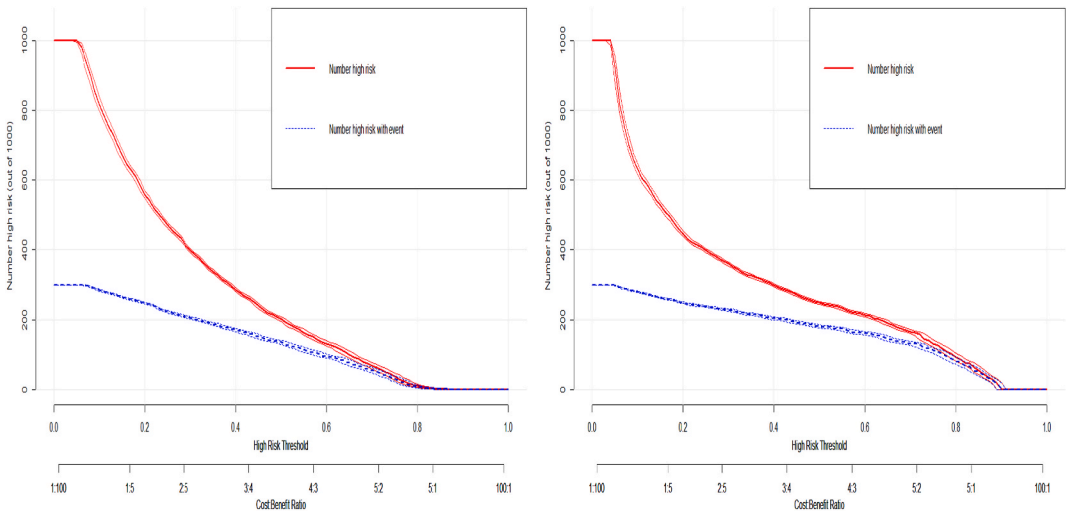

Fig. 6. (a)Community indifference curve of neural network and nomogram.(b) Community indifference curve of neural network and nomogram.

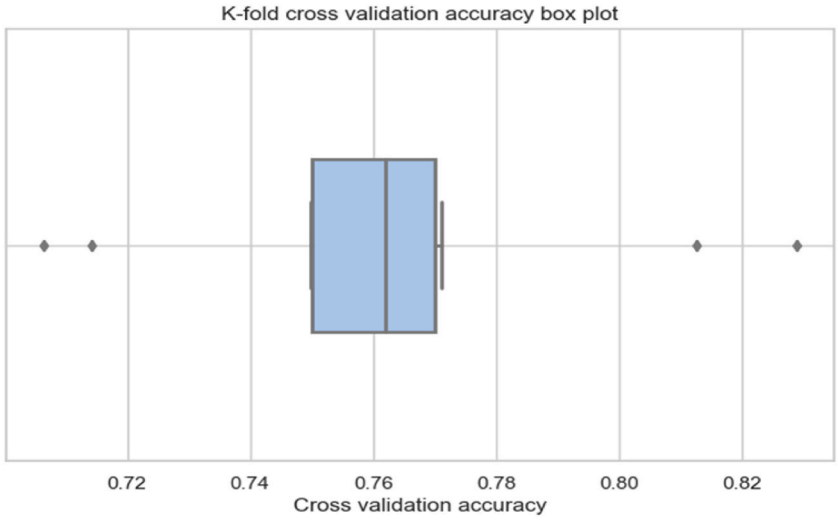

Fig. 7. K-fold cross validation box diagram.

increasingly prevalent. Although osteoporosis and osteopenia greatly increase bone fragility [13], they do not cause any evident symptoms in the early stage; therefore, they are not diagnosed until complications such as spinal or limb fractures occur [14], which seriously affect patients' health condition and quality of life, necessitating the importance of timely diagnosis and treatment of osteoporosis and osteopenia in the early stage [15]. Many studies have applied algorithms and evaluation tools based on public awareness of osteoporosis and osteopenia risk factors such as age, sex, family history of patients' fractures, use of glucocorticoids and vitamin D, blood calcium, and other indicators [16] such as fracture risk assessment tool in the clinical setting [17,18], which indeed provides a reference to assess the risk of bone mineral density abnormalities in a certain population [19], but the evidence is not comprehensive. Taking the American population as an example, this study included the intake of carbohydrates, dietary fiber, coffee, and other dietary components, as well as the levels of electrolytes such as blood phosphorus, blood potassium, and blood sodium, which may be deficient in abnormalities, as research factors; next, the neural network and nomogram were integrated to establish a prediction model to provide a reference for people who are accustomed to consuming carbohydrates, dietary fiber, coffee, and other dietary components. This study used data extracted from the NHANES database for analyses, which includes data from the multi-ethnic American population. In the American population, the usual diet of only Asian people includes carbohydrates and dietary fiber, whereas that of other populations includes meat fat, processed drinks, and milk [20,21]. Therefore, research on the relationship between the intake of carbohydrates and dietary fiber and the development of osteoporosis and osteopenia is very limited, and this study will be of particular significance as a reference for the American population.

This study collected data on patients' sex, age, height, weight, BMI, family history of parents' fracture, race, carbohydrate intake, dietary fiber consumption, vitamin D, caffeine, blood phosphorus, potassium, sodium, and calcium to compare the general characteristics between the abnormal bone mineral density group and the normal bone mineral density group. Compared with the normal bone mineral density group, the abnormal bone mineral density group had increased age, carbohydrate, coffee intake, phosphorus, and potassium but reduced vitamin D, height, weight, BMI, dietary fiber, and blood sodium; additionally, female sex, family history of parents' fracture, and race were related to the development of bone mineral density abnormalities, which is consistent with the findings of previous studies [22,23]. However, only a few studies have assessed the intake of carbohydrates, dietary fiber, and coffee, as well as the levels of various electrolytes other than blood calcium; hence, further analysis should evaluate these aspects.

This study revealed that the important risk factors for bone mineral density abnormalities were coffee intake, carbohydrate consumption, BMI, height, blood sodium, blood calcium, blood phosphate, blood potassium, dietary fiber, vitamin D use, age, weight, race, family history of parents' fracture, and sex. It is worth noting that coffee intake and carbohydrate consumption are the top two important risk factors, and the proportion of importance is more than 90 %. However, because the neural network could not provide the relevant interpretation of the calculation results, the nomogram was further used for analysis.

The nomogram screened using logistic regression analysis [24] is a widely used clinical prediction model that can assign risk scores and quantitative indices and has a high clinical value [25]. The risk factors revealed by the nomogram used in this study include age, sex, coffee intake, dietary fiber, carbohydrate consumption, height, BMI, blood phosphate, blood potassium, and blood sodium. BMI had the highest score, followed by coffee intake, dietary fiber, blood phosphate, and blood potassium, all of which showed higher scores. In addition to common risk factors such as low BMI and low height, increased coffee and carbohydrate intake, decreased dietary fiber intake, and the consequent reduction in blood phosphorus and sodium and elevation in blood potassium will promote the formation of an abnormal bone mineral density, and the probability of risk can be obtained by adding the scores. The results of the nomogram analysis are beneficial for the prediction and evaluation of the algorithm in terms of dietary structure.

Due to the wide range of carbohydrates, there is no directly related mechanism of action for reference. However, according to a recently published study, the relationship between carbohydrate containing food intake and bones is involved. In 2019, Matsuzaki

[26] and colleagues evaluated the impact of brown rice intake on BMD within a year. The research results indicate that compared to the group eating white rice, the group eating brown rice showed significant changes in bone area.However, there are no other studies in the literature that consider the correlation between the evaluation of BMD and the consumption of carbohydrate foods such as rice, pasta, or bread and its derivatives.

The increase in caffeine intake leading to abnormal bone mineral density may be related to the deterioration of human calcium balance. The study conducted by Yeh J et al. [27]. on a mouse model showed that in the case of impaired calcium absorption capacity, daily caffeine intake for four consecutive weeks can lead to changes in calcium balance. The study also speculates that this situation may exist in elderly people, as their ability to synthesize 1,25- (OH) 2D decreases. A high dietary fiber diet is beneficial for bone metabolism and may be regulated by the composition of the microbiota: a recent narrative review summarizes the results of preclinical studies that support the positive impact of gut microbiota on bone mineral density and strength parameters [28]., And a previous study also suggests that the intake of vegetables and fruits can reduce osteoporosis development to a certain extent [29]. The effect of the same electrolyte on osteoporosis and osteopenia may be realized through the maintenance of a long-term dietary structure. For example, this study suggests that high potassium and low phosphorus and sodium promote the onset and development of osteoporosis and osteopenia. Low sodium concentration is a risk factor for osteoporosis in postmenopausal women [30], but the specific mechanism remains unknown. Low phosphorus concentration is related to the occurrence of secondary osteoporosis [31].

Further research analysis shows that the electrolyte situation in the human body is generally maintained within a certain range for a long time [32], which is known as human homeostasis.According to Mariangela Rondanelli et al. [7], electrolyte conditions can have a significant impact on bone metabolism.Further research suggests that a decrease in blood sodium will promote the occurrence and development of osteoporosis and bone loss, possibly related to the metabolism of hydroxyproline (an amino acid derivative contained in collagen) and parathyroid hormone (involved in calcium metabolism), which participate in the process of bone metabolism in this way [33]. Similarly, chronic phosphorus deficiency will lead to bone demineralization and loss of Bone resorption, Long term dietary phosphorus deficiency can lead to delayed growth and development in children, as well as similar adult osteomalacia, as phosphorus deficiency can lead to the release of calcium from bones and hypercalciuria [34,35]. The impact of increased blood potassium on bone metabolism is also related to the direct effects of alkaline load and potassium ions, as acid load has a positive impact on bone mineral density absorption [36,37].

Finally, the ROC curve, calibration curve, DCA, and CIC were used to verify and evaluate the results of neural network and nomogram analyses, which suggested that the two algorithms had good accuracy in screening the risk factors for bone mineral density abnormalities. The AUC value of the neural network ROC curve [38] was 85.8 %, indicating a high predictive value. Moreover, the calibration curve [39] indicated that the consistency in the prediction probability, the observed event occurrence rate, and the result frequency are not much different between the two algorithms, and the discrimination ability is good. DCA analysis [40] indicated that the two algorithms have a clinical net benefit rate of below 80 % of the prediction probability, and CIC analysis more intuitively showed the relationship between high risk and high risk with an event. The combination of the two algorithms can be used to test the clinical practicability of the model. The neural network and nomogram combination has better clinical practicability and is useful for application in clinical and epidemiological studies.Finally, internal validation of the neural network was conducted, and the cross validation results showed that the neural network had a certain degree of accuracy.

There are shortcomings in this study, such as statistical analysis based on databases, which can partially indicate epidemiological patterns. The specific mechanism of action needs to be further confirmed through laboratory research.

In addition, the research factors included in this article are still insufficient. In the future, various diets such as milk, tea, and various beverages can be included in further research, and more types of electrolytes such as blood magnesium and blood chlorine can be added.

At the same time, because the NHANES database is a public database with a relatively complete and extensive independent variable factors and a large data population, which is difficult to fully replicate for single center studies, there is currently no external validation in this article. The future research focus should be on validating this study based on multicenter, larger number of variable factors, and larger population studies. This study is more applicable to the American population, as the American population is multi-ethnic, while most other countries have a single ethnic group as the main body, it is also a shortcoming of this study.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/Supplementary Material.

Ethics statement

The studies involving human participants were reviewed and approved by Protocol #2020-12. The patients/participants provided their written informed consent to participate in this study.

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Author disclaimer

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CRediT authorship contribution statement

LuWei Li: Conceptualization, Data curation, Formal analysis, Supervision, Validation, Writing – original draft, Writing – review & editing. **SiShuai Cheng:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **GuoQuan Xu:** Data curation, 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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20677.

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