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Association study on bone metabolism in type 2 diabetes by using machine learning

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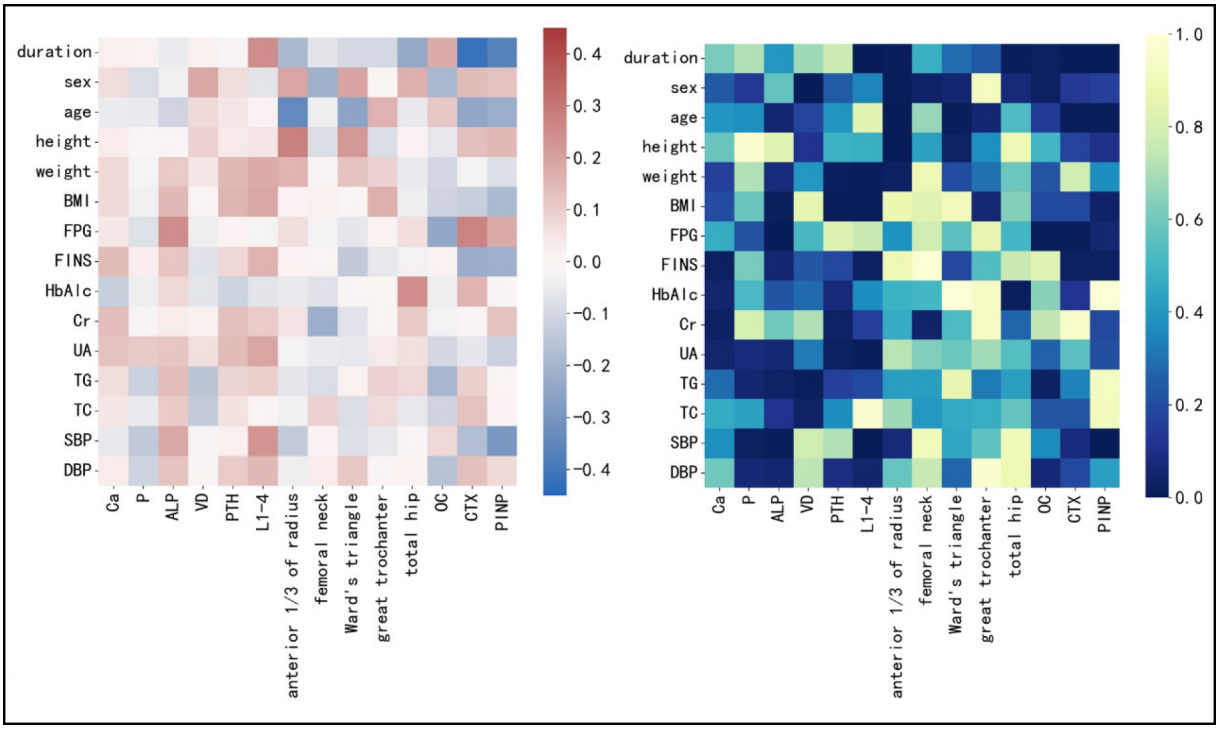
Graphical abstract



Thermodynamic diagram of the multiple linear regression equation coefficient and p value.

Public summary

- In-depth analysis of type 2 diabetes in Anhui Province suggested that the risk factors for bone complications included body shape indexes, creatinine, uric acid, triglycerides and blood pressure.
- Interestingly, the bone mineral density of lumbar vertebrae in patients with type 2 diabetes was increased, suggesting that there was a risk of lumbar hyperosteogeny.

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Abstract: Type 2 diabetes mellitus is often accompanied by serious complications, including bone metabolic diseases, liver diseases, and kidney diseases, which are affected by the course of disease, sex, age and individual differences and cannot be a unified treatment paradigm. Therefore, for the in-depth analysis of clinical data, looking for the correlation of type 2 diabetes complication data has important guiding significance for the treatment of type 2 diabetes and its complications. In this paper, multiple linear regression models were established based on the clinical data of type 2 diabetes patients in Anhui Province. Our results suggest that the main factors affecting bone complications of type 2 diabetes include body shape indexes, creatinine, uric acid, triglycerides and blood pressure. Interestingly, the bone mineral density of lumbar vertebrae in patients with type 2 diabetes was increased, suggesting that there was a risk of lumbar hyperosteogeny.

Keywords: type 2 diabetes; machine learning; multiple linear regression (MLR); bone metabolism

CLC number: R587.2 **Document code:** A

1 Introduction

Type 2 diabetes mellitus (T2DM) is a serious chronic disease with a variety of causes, mainly related to genetic factors, diet, lifestyle and the endocrine system. Clinical examination of diabetes mellitus includes fasting glucose, fasting insulin levels and glycosylated hemoglobin levels, which can reflect the average blood sugar status of the human body in the last three months. Type 2 diabetes refers to the normal production of insulin, but it cannot clear blood sugar in the human body, resulting in long-term high blood glucose. Long-term high blood glucose levels can cause serious damage to many organs of the human body and even induce life-threatening complications, such as visual impairment, poor healing of lower limb ulcers, heart disease, osteoporosis or stroke[1,2].

Lipocalin disorders are a common comorbidity of type 2 diabetes. It is characterized by hyperlipidemia and increased blood cholesterol and triglyceride levels, resulting in fatty liver and even cirrhosis. Alkaline phosphatase is usually used to evaluate whether the liver parenchyma is seriously damaged[3]. The impact of diabetes on the kidney is also very obvious. Early diabetic nephropathy can be reversed; however, once clinical proteinuria occurs, it can only delay its further development. Creatinine needs to be filtered through the kidneys, and very little is reabsorbed through the kidneys[4]. Uric acid is metabolized by the kidneys. Both creatinine and uric acid levels are used clinically to reflect the detoxification ability of the kidney[4]. Diabetes mellitus and hypertension are both related to hyperlipidemia, and there may be common genetic genes. In addition, high blood sugar, high blood viscosity, vascular wall damage and vascular resistance changes are factors that easily cause hypertension in diabetic patients[5]. Systolic blood pressure and diastolic blood pressure together reflect the blood pressure of patients.

Diabetic osteoporosis is another important complication of diabetes mellitus in the skeletal system. As a systemic skeletal disease, its main characteristics are the reduction of bone mass and the damage of bone tissue structure[6]. Interestingly, while type 2 diabetes is often linked with preserved bone mineral density, it is also associated with increased skeletal fragility. This paradoxical relationship further complicates the clinical assessment and management of bone health in T2DM patients, making traditional fracture risk calculations often inadequate for this group[7]. Due to the increasing number of diabetic patients each year, diabetic osteoporosis has become one of the important reasons for the decline in daily life varieties of the diabetic population, and it is also one of the diseases with the greatest risk to the elderly and has received increasing attention from scholars in recent years. The changes

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in calcium and phosphorus metabolism are reflected in the changes in bone morphology, structure and tissue composition to varying degrees[6]. 25-Hydroxyvitamin D3 is an important substance for bone formation by conserving calcium into bone. Serum bone gla protein (S-BGP) is a specific index to evaluate bone formation and the bone turnover rate[8]. Vitamin D is a fat-soluble vitamin that plays an important role in controlling calcium levels and bone calcification, which stimulates the release of parathyroid hormone[6]. The main effect of parathyroid hormone is to promote osteopenia and increase blood calcium levels[6]. Alkaline phosphatase is also a marker of bone metabolism that can reflect the condition of the human skeleton. It is an index to detect the metabolic activity of cartilage and bone tissue in blood[3]. Osteocalcin is critical for the osteogenic capacity of osteoblasts, and its main function is to promote bone formation[6]. Beyond its structural functions, recent findings suggest that bone, as an endocrine organ, releases osteocalcin alongside other hormones, playing a role in glucose metabolism and potential implications in diabetic complications[9]. The N-terminal pro-peptide of type I procollagen is an index reflecting the content of collagen in bone[10]. If the N-terminal propeptide of type I procollagen decreases, collagen decreases, and bone metabolism is weak[10]. The level of β-Cross Laps is a potent marker for metabolic bone diseases characterized by markedly enhanced osteoclast activity[11].

Although there have been some reports on the clinical data analysis of T2DM, the existing data models cannot accurately predict the correlation of clinical indexes in different regions because of the different pathogenesis of T2DM, the diverse causes and the significant differences in the distribution of population data in each region. Machine learning methods can mine medical information conveniently and noninvasively and have a strong ability to process large-scale medical data quickly. In the present study, we established a classification model based on the clinical datasets of T2DM patients in Anhui Province and deeply analyzed the correlation between bone metabolism and other indexes of T2DM patients, which provides important reference data for potential early screening and prevention and treatment.

2 Subjects and methods

To study the interaction between bone metabolism data and other data of type 2 diabetes patients, we used multiple linear regression (MLR), support vector regression (SVR) and other machine learning methods to mine and analyze the clinical data of patients. The pipeline of this study is shown in Fig. 1. First, 282 clinical data points of type 2 diabetes patients were collected, and the outliers in the data were cleaned by the boxplot method. Then, the missing values were filled by K-nearest neighbors (KNN). On the basis of the preprocessed data, multiple linear regression was used to analyze the relationship between the indexes one-to-one. The independent variable indexes of the multiple linear regression model were screened through the analysis results. According to the results of data screening, the multiple linear regression model and support vector regression model were built again, and the reliability of data screening was improved by model scoring. We used Python (version 3.8) to implement boxplots, KNN, MLR, and SVR. We also used Python and Excel for data visualization.

2.1 Subjects

All the data in this study were collected from the First Affiliated Hospital of USTC, which included 282 diabetic patients with 29 indexes. The use of clinical data obtained ethical approval from the Ethics Committee of the First Affiliated Hospital of USTC (Approval No. 2020-KY-38). The indexes and their abbreviations are shown in Table 1. The 29 indexes measured by patients in the dataset can be divided into several categories: general physical examination, routine examination of diabetes mellitus, blood lipids and bone metabolism detection.

2.2 Multiple linear regression

Multiple linear regression is mainly used to evaluate the relationship between the dependent variable and multiple independent variables[12,13]. We built an MLR model with bone metabolism indicators as independent variables and other data as dependent variables.

The MLR model can be expressed as:

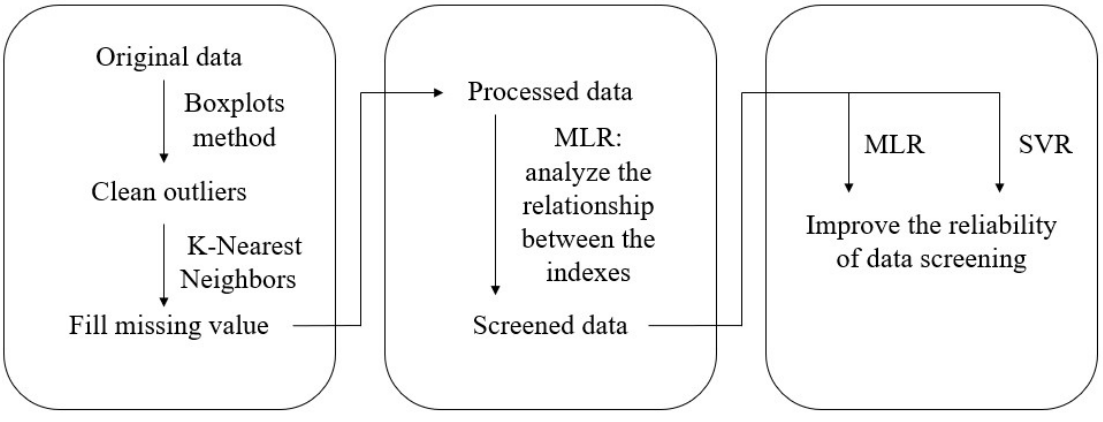

Fig. 1. The pipeline of MLR and SVR models for clinical datasets.

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Table 1. Indexes and their abbreviations and categories.

Categories			Indexes	Abbreviations
General physical examination			Sex	
			Age	
			Height	
			Weight	
			Body mass index	BMI
Routine examination of diabetes mellitus			Duration	
			Fasting plasma glucose	FPG
			Fasting insulin	FINS
			Glycosylated hemoglobin	HbAlc
Liver and kidney function			Creatinine	Cr
			Uric acid	UA
			Alkaline phosphatase	ALP
Blood lipids			Triglyceride	TG
			Total cholesterol	TC
Blood pressure			Systolic blood pressure	SBP
			Diastolic blood pressure	DBP
Bone metabolism detection	Bone mineral density detection		Lumbar L1–4 bone mineral density	L1–4
			Bone mineral density at the junction of radius and distal 1/3 of ulna	Anterior 1/3 of radius
			Bone mineral density of femoral neck	Femoral neck
			Bone mineral density in Ward's triangle	Ward's triangle
			Great trochanter bone mineral density	Great trochanter
			Bone mineral density at the total hip	Total hip
	Bone metabolism markers detection	General biochemical markers	Serum calcium	Ca
			Serum phosphorus	P
		Bone metabolism regulating hormones	Vitamin D	VD
			Parathyroid hormone	PTH
		Bone formation markers	Alkaline phosphatase	ALP
			Osteocalcin	OC
			Propeptide of type I procollagen	PINP
		Bone resorption markers	β-Cross Laps	CTX

$$\boldsymbol{Y}=\boldsymbol{X}\boldsymbol{\beta}+\boldsymbol{\varepsilon},$$

$$\boldsymbol{Y}=\begin{pmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{pmatrix}, \boldsymbol{X}=\begin{pmatrix} 1 & X_{11} & \cdots & X_{1k} \\ 1 & X_{21} & \cdots & X_{2k} \\ \vdots & \vdots & & \vdots \\ 1 & X_{n1} & \cdots & X_{nk} \end{pmatrix},$$

$$\boldsymbol{\beta}=\begin{pmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_k \end{pmatrix}, \boldsymbol{\varepsilon}=\begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{pmatrix},$$

where $\boldsymbol{Y}$ is the dependent variable, $\boldsymbol{X}$ is the design matrix and is assumed to be of full column rank (linear independence between variables), $\boldsymbol{\beta}$ is the parameter vector, and the residual vector $\boldsymbol{\varepsilon}$ satisfies the previous assumptions.

To comprehensively analyze the relationship between the indexes, we built 15 multiple linear regression models with 14 bone metabolism indexes as independent variables and 15 other data as dependent variables. The relationship between the bone metabolism index and other data can be mined more pertinently by linearly fitting other kinds of data with the bone metabolism index.

2.3 Statistics

Before analyzing the role of different bone metabolism data in fitting other indexes through the MLR model, it is necessary to carry out the F test on the MLR model to determine the overall significance of the linear equation. The F test is a test in which the statistic follows the F-distribution under the null hypothesis (H0). It is usually used to analyze statistical models with more than one parameter (such as MLR) to determine whether some or all of the parameters in the model are suitable for estimating the dependent variable.

Therefore, the original hypothesis (H0) that all regression coefficients are 0 and the alternative hypothesis (H1) that all regression coefficients are not 0 are proposed. Under the

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condition that the null hypothesis is true, the following statistics can be established:

$$F = \frac{\mathrm{SSR}/k}{\mathrm{SSE}/(n-k-1)},$$

where SSR is the regression sum of squares and SSE is the residual sum of squares. This statistic obeys $F(k, n-k-1)$. F can be obtained from the sample index value. Given the significance level α, the critical value $F_\alpha(k, n-k-1)$ can be obtained by looking up the table. If $F > F_\alpha(k, n-k-1)$, the original hypothesis is rejected, and the multiple linear regression model is considered to be significant overall; if $F \leqslant F_\alpha(k, n-k-1)$, the original hypothesis is accepted, and the model is considered to be not significant overall.

We performed an F test on the multiple linear regression model to determine the overall significance of the linear equation.

Then, other types of indexes were linearly fitted by bone metabolism indicators, and the regression parameters were tested by t test. Combined with regression parameters and t tests, the relationship between bone metabolism indicators and other data was explored.

The result of the t test is expressed as a p value, which usually indicates that the independent variable is strongly explanatory of the dependent variable when it is below 0.05.

2.4 Stepwise multiple linear regression

After establishing the regression equation, we selected the optimal regression subset from the set of relevant independent variables by the stepwise regression method. First, we selected the independent variable with the largest p value in the MLR model and remove the independent variable from the independent variable set. Then, the MLR model was built again with the deleted subset of independent variables. The final MLR model was obtained until the p values of the t tests of all independent variables were less than 0.05.

2.5 Support vector regression

To further verify the relationship between bone metabolism indicators and other data, bone metabolism indicators were screened according to the results of the t test. The new MLR and SVR models were built by using the new indexes obtained by screening and compared with the model built by using all bone metabolism indexes. The evaluation strategy of the SVR model is described as follows: the dataset was randomly divided into five equal parts without repetition, and the best parameters of the SVR were found by fivefold cross-validation and grid search, in which the mean value of R2 on the validation set calculated by cross-validation under the found best parameters was used as the score of the SVR model.

3 Results and discussion

3.1 Statistical significance analysis

In this paper, 15 multivariate linear regression models were established, with 14 bone metabolism indexes as independent variables and 15 other examination indexes as dependent variables. The calculation results of the F-statistic are shown in Fig. 2. Except for two models with Cr and TC as dependent variables, most of the models were considered statistically significant at a significance level of 0.05 and could be further analyzed.

3.2 Relationship between bone metabolism indexes and other examination indexes

The overall relationship between bone metabolism indexes and other examination indexes is shown in Fig. 3.

3.2.1 General physical examination indexes

Sex was positively correlated with vitamin D and anterior 1/3 of radius (p<0.05) and negatively correlated with femoral neck and osteocalcin (p<0.05). Age was negatively correlated with the anterior 1/3 of radius (p<0.05), Ward's triangle (p<0.05), CTX (p<0.05) and PINP (p<0.05). Height was positively correlated with the anterior 1/3 of radius (p<0.05) and Ward's triangle (p<0.05). Body weight was positively

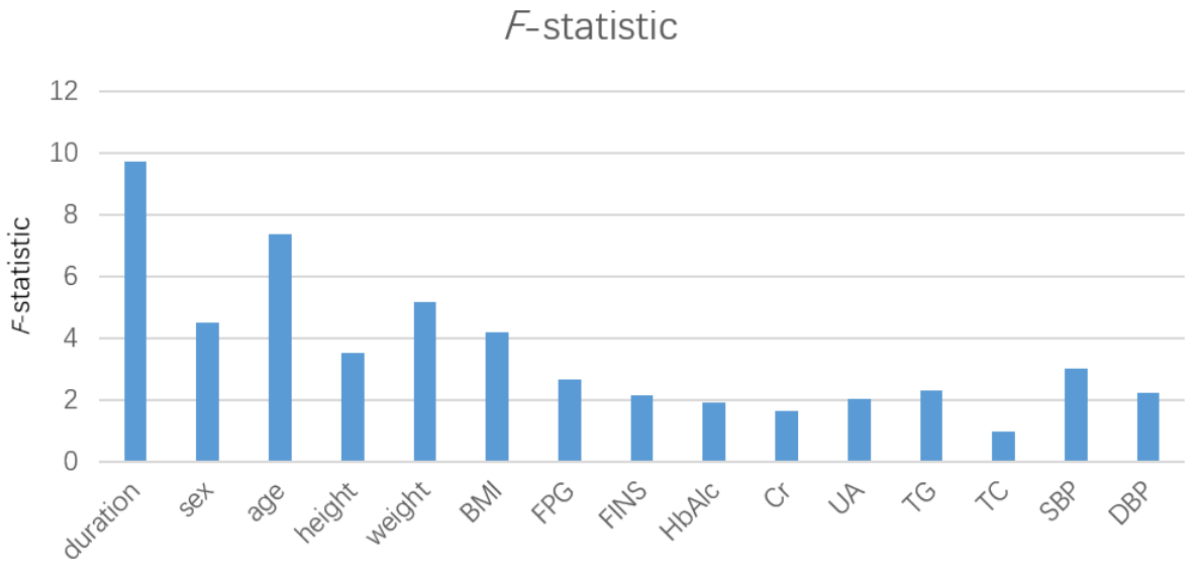

Fig. 2. F-statistic in the multivariate linear regression model.

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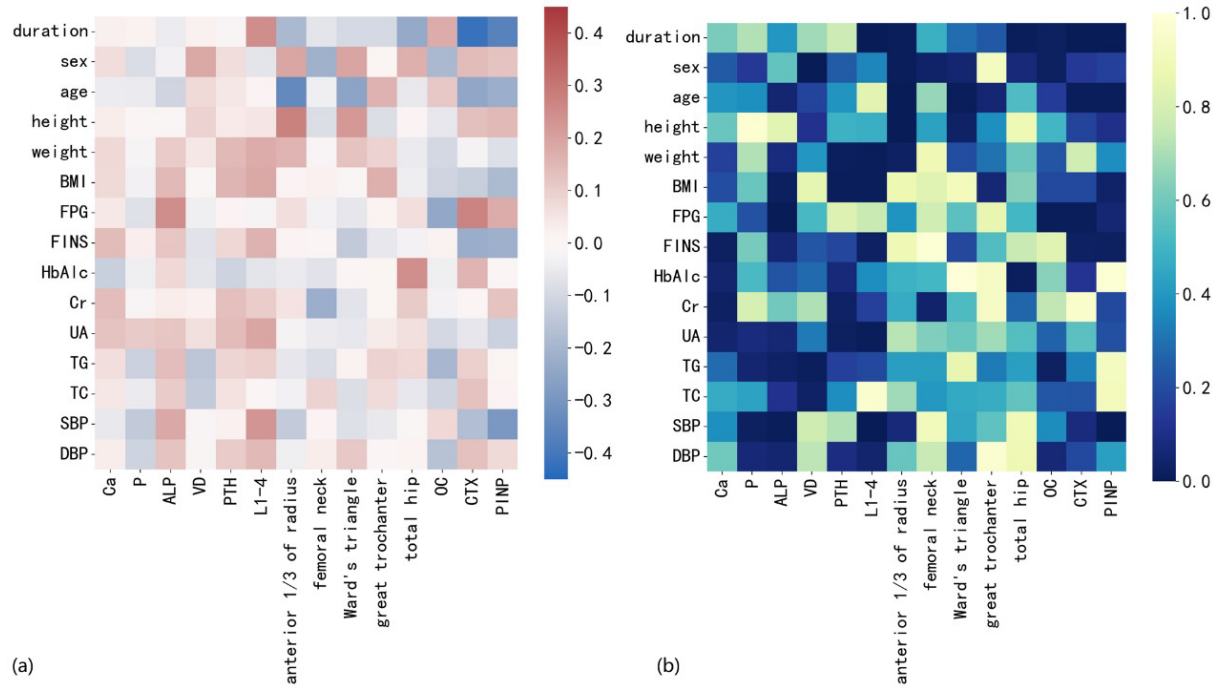

Fig. 3. (a) Thermodynamic diagram of multiple linear regression equation coefficient (red represents positive correlation, blue represents negative correlation, and the darker the color, the larger the absolute value of the coefficient); (b) p value thermodynamic diagram of bone metabolism index and other data (the darker the color, the smaller the p value).

correlated with parathyroid hormone (p<0.05), L1-4 (p<0.05) and anterior 1/3 of radius (p<0.05). BMI was positively correlated with vitamin D (p<0.05), parathyroid hormone and L1-4 (p<0.05) and negatively correlated with PINP (p<0.05).

By using multiple linear regression analysis of the relationship between bone metabolism indexes and other indexes, BMI, height, weight and other indexes of body shape were generally positively correlated with bone mineral density, indicating that the control of weight and BMI in patients with type 2 diabetes mellitus was particularly important for the treatment of osteoporosis. The relationship between the indexes of routine physical examination and bone metabolism is usually indirect. With increasing age after menopause, estrogen levels decrease, which results in increased production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in the anterior pituitary through the negative feedback regulatory mechanism of the hypothalamus-pituitary. García-Martín et al.[14] found that FSH and LH were positively correlated with osteocalcin and β-CTX. This finding is inconsistent with the conclusion that age is negatively correlated with CTX in this paper. Deficiency of vitamin D and parathyroid hormone is associated with bone loss, increased bone resorption, and increased fracture risk in elderly individuals. PINP, as an extracellular breakdown product when osteoblasts synthesize and release procollagen fibers, can be used as a marker of bone cell activity and bone formation level and a biochemical index highly related to osteoporosis[15]. Shan et al.[16] confirmed that low BMI may be associated with osteoporosis in postmenopausal women with type 2 diabetes. This is consistent with the results in this paper.

3.2.2 Routine examination indexes of diabetes mellitus

The course of disease was positively correlated with L1-4 and osteocalcin (p<0.05) and negatively correlated with anterior 1/3 of radius (p<0.05), total hip (p<0.05), CTX (p<0.05) and PINP (p<0.05). Fasting blood glucose levels were positively correlated with alkaline phosphatase (p<0.05) and CTX (p<0.05) and negatively correlated with osteocalcin (p<0.05). Fasting insulin was positively correlated with calcium and L1-4 (p<0.05) and negatively correlated with CTX (p<0.05) and PINP (p<0.05). Glycosylated hemoglobin was positively correlated with total hip circumference (p<0.05) and negatively correlated with calcium (p<0.05).

Im et al.[17] found that the level of osteocalcin in patients with type 2 diabetes was significantly lower than that in non-diabetic patients and people with impaired glucose tolerance, which is consistent with our results. Insulin can promote the synthesis of vitamin D and further promote the secretion of osteocalcin by osteoblasts. Furthermore, osteocalcin can be expressed in osteoblasts and released into the blood to maintain glucose homeostasis by stimulating the expression of insulin in the pancreas, thereby alleviating the symptoms of glucose intolerance[18]. In addition, Rossini et al.[19] believed that insulin receptors on osteoblasts could not bind to insulin due to insufficient insulin in diabetic patients, which affected the uptake of amino acids and collagen fibers by osteoblasts, resulting in a decrease in osteocalcin secretion. Indeed, we found that fasting blood glucose levels are negatively correlated with osteocalcin. As a regulatory factor of bone formation, insulin can promote the synthesis of collagen, cellular amino acids and nucleotides, and stimulate the reproduction of bone cells[20], thereby reducing bone loss and maintaining bone mass. The expression level of PINP reflects the formation of new bone, and the faster the formation of new bone, the more PINP in the blood[10]. This is contradictory to the result that fasting insulin is negatively correlated with CTX

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and PINP.

3.2.3 Renal function tests

Creatinine was positively correlated with calcium (p<0.05) and parathyroid hormone (p<0.05) and negatively correlated with the femoral neck (p<0.05). Uric acid was positively correlated with calcium, parathyroid hormone (p<0.05) and L1-4 (p<0.05).

Diabetes-related indexes were positively correlated with uric acid levels and lumbar spine L1-4, indicating that there is not only the risk of osteoporosis but also the phenomenon of lumbar disc hyperplasia in the complications of type 2 diabetes mellitus. The possible reason for hyperplasia can be the enrichment of high uric acid in lumbar bone metabolism, suggesting that the pathological characteristics of lumbar disc hyperplasia and osteoporosis should be considered comprehensively in clinical treatment. Previous studies have reported that urinary creatinine is helpful for the analysis of bone metabolism indexes[21], yet there are relatively few studies on serum creatinine. Keizman et al.[22] showed that hyperuricemia may be incompatible with osteoporosis, and patients with hyperuricemia are less likely to develop osteoporosis. As an antioxidant produced inside the body, uric acid can not only chelate metal ions but also scavenge peroxides and oxygen free radicals, further inhibiting osteoclastogenesis[23], thereby reducing the occurrence of osteoporosis. This study also found a positive correlation between uric acid and lumbar spine bone mineral density.

3.2.4 Blood lipid examination index

Triglycerides were positively correlated with alkaline phosphatase (p<0.05) and negatively correlated with vitamin D (p<0.05) and osteocalcin (p<0.05). Total cholesterol was negatively correlated with vitamin D (p<0.05).

Studies on the relationship between blood lipid indexes and bone metabolism indexes are contradictory. Clinical studies indicated that the BMD of lumbar vertebrae was negatively correlated with HDLC in different sexes[24], and vitamin D was inversely associated with the risk of obesity and metabolic syndrome[25]. Similarly, an in vitro study indicated that lipoprotein oxidation products can inhibit the differentiation of bone marrow stem cells into osteoblasts and promote their differentiation into osteoclasts[26]. However, Go et al.[27] reported that lumbar spine BMD was not associated with total cholesterol, low-density lipoprotein cholesterol (LDLC), or high-density lipoprotein cholesterol (HDLC) in postmenopausal women. In the present study, we found that both triglycerides and cholesterol are negatively associated with vitamin D, which prevents bone resorption and bone loss. OCN is an indicator of osteoblasts and is negatively related to blood lipids. The results suggest that increased blood lipids will increase the risk of osteoporosis in type 2 diabetes.

3.2.5 Indexes of blood pressure examination

Systolic blood pressure was positively correlated with alkaline phosphatase (p<0.05) and L1-4 (p<0.05) and negatively correlated with P (p<0.05) and PINP (p<0.05). Diastolic blood pressure was positively correlated with anterior 1/3 of radius (p<0.05).

Thus far, the relationship between hypertension and bone metabolism is not clear. He et al.[28] found that the bone mineral density in the trigone of patients with hypertension is lower, suggesting that there is a correlation between hypertension and bone mineral density in the elderly. However, we found that cardiovascular indexes such as blood lipids and blood pressure were positively correlated with bone mineral density, suggesting that attention should be given to bone health while treating type 2 diabetes-induced cardiovascular diseases.

3.3 Stepwise multiple linear regression

The final equation coefficient of stepwise multiple linear regression is shown in Fig. 4. Generally, age and blood lipid indexes are negatively correlated with bone factors, while height and kidney function represent a positive correlation with bone metabolism in diabetic patients. Other indicators, i.e., Weight, BMI, routine examination of diabetes mellitus, and blood pressure presented mixed effects on bone factors. Interestingly, PTH, anterior 1/3 of radius and Ward's triangle bone showed clear sex differences, suggesting that bone metabolism can be regulated by sex hormones in type 2 diabetes. Cai et al.[8] found that the S-BGP level was significantly negatively correlated with age, which indirectly proved that age was negatively correlated with bone metabolism. This is consistent with the results obtained in this paper. Although previous studies have shown that blood lipid effects on bone metabolism are contradictory, we again showed that blood lipids were negatively correlated with bone formation in type 2 diabetes. Uric acid, the end product of purine metabolism, is excreted predominantly by the proximal tubules. Our results showed that uric acid levels are positively correlated with L1-4, which is significantly increased in diabetic patients. This suggests that the risk of lumbar disc hyperplasia can be induced by the local accumulation of uric acid, and further studies are needed to fully understand the variety of bone metabolism in type 2 diabetes.

3.4 Validate index relationships

To further prove the relationship obtained by t test analysis between the bone metabolism indexes and other data, we screened the bone metabolism indexes according to the reliability results of the t test and then re-established a multiple linear regression model using the new indexes obtained by screening and compared it with the original models using all the bone metabolism indexes. Cr and TC models after screening were also considered statistically significant at a significance level α of 0.05.

Because the number of independent variables of the model has changed after screening and the corresponding parameters of the F distribution have also changed, we cannot directly compare the explanatory degree of the model by comparing the F value; alternatively, we choose the p value obtained by the F test to evaluate the credibility of the model. After screening, except for the BMI model, the p values of other models were generally lower than those before screening (Table 2), indicating that the credibility of the model was further improved.

By analyzing the difference between the predicted scores of

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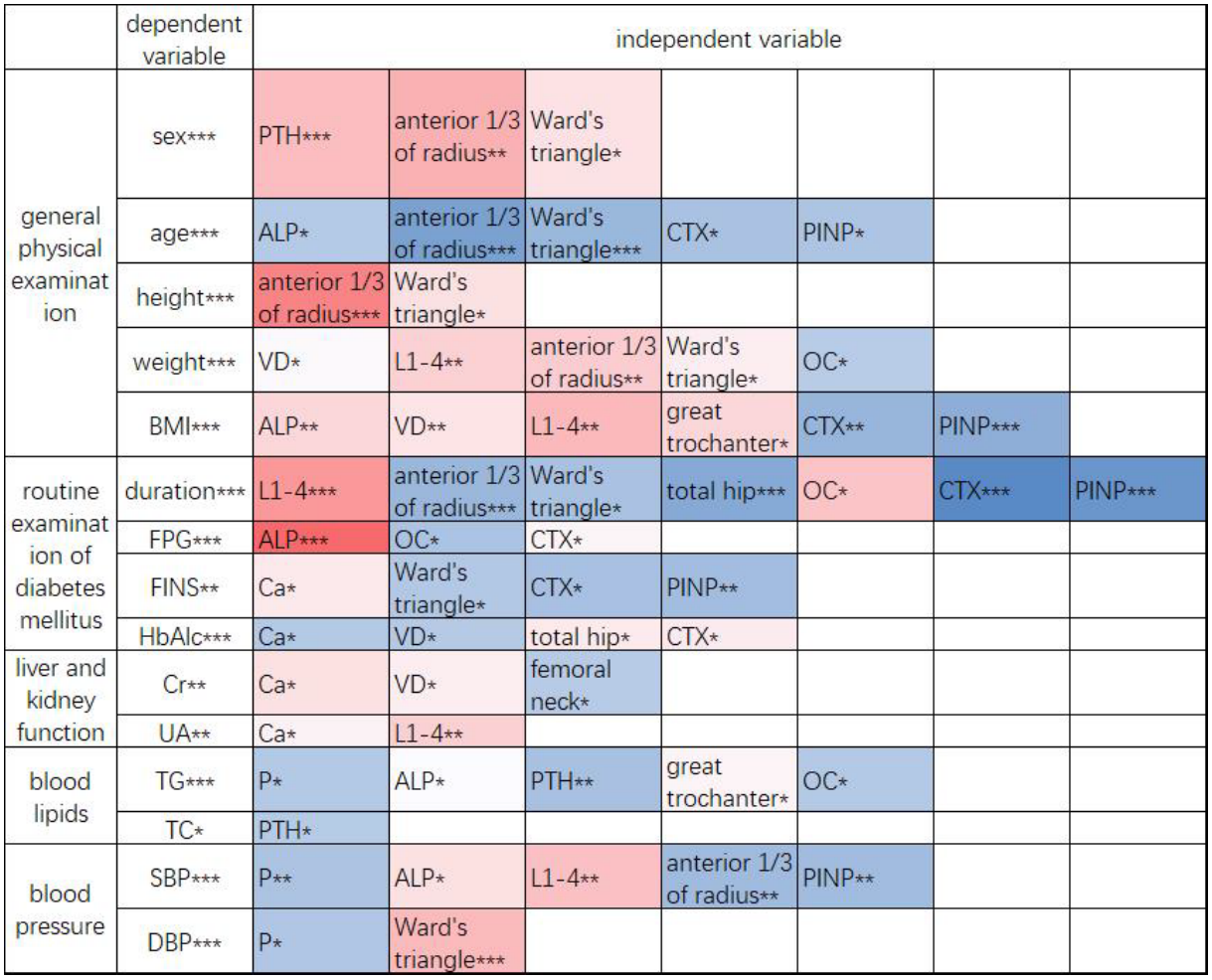

Fig. 4. Thermodynamic diagram of the final equation coefficient of stepwise multiple linear regression. Red represents a positive correlation, and blue represents a negative correlation. The darker the color is, the larger the absolute value of the coefficient. *: $p<0.05$,**: $p<0.01$,***: $p<0.001$.

Table 2. p value of the linear regression model before and after screening.

	p value before screening	p value after screening
Duration	1.84E−17	1.23E−20
Sex	2.66E−07	1.21E−08
Age	5.00E−13	3.25E−15
Height	2.59E−05	4.73E−09
Weight	1.25E−08	1.15E−10
BMI	1.16E−06	1.72E−06
FPG	0.001236	2.73E−06
FINS	0.010084	0.008761
HbAlc	0.025417	0.008435
Cr	0.068152	0.002536
UA	0.016424	0.002239
TG	0.004820	0.001371
TC	0.487058	0.033990
SBP	0.000247	6.51E−05
DBP	0.006726	0.000282

bone metabolism indexes with a strong explanation and the predicted scores of all bone metabolism indexes (as shown in Fig. 5), we showed that the scores of most data improved, which further proves the effectiveness of multiple linear regression analysis.

3.5 Geographical limitations

While our study offers valuable insights into the relationship between bone metabolism indexes and other associated factors, it is important to note a significant limitation concerning the source of our samples. All samples in our study originated exclusively from Anhui Province, which may influence the generalizability of our findings. As a specific geographic region, Anhui Province might possess certain regional factors, such as dietary habits, lifestyles, and genetic predispositions, that could be linked with bone metabolism indexes and might impact our research results.

We recognize that having a validation dataset from different regions is crucial to corroborate our findings. However, due to constraints such as resource availability and time, we were unable to obtain and analyze such a dataset in this study. In the future, we plan to expand our sample base to include participants from other areas to ensure broader applicability of our findings.

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Fig. 5. Differences in support vector regression model scores before and after screening.

4 Conclusions

In the present study, we used multiple models to predict the relationship between bone metabolism and other indexes in type 2 diabetes and found that the control of weight and BMI in patients with type 2 diabetes mellitus is particularly important for the treatment of osteoporosis. Moreover, there is a positive correlation between diabetes-related indicators and uric acid levels and lumbar L1-4, indicating that there is not only the risk of osteoporosis but also the phenomenon of lumbar disc hyperplasia in the complications of type 2 diabetes mellitus. Despite these insights, it is essential to acknowledge that our sample pool was limited to Anhui Province, potentially impacting the broader applicability of our findings. Therefore, in clinical practice, both the pathological characteristics of lumbar disc hyperplasia and osteoporosis and the potential influence of regional factors on bone metabolism should be taken into account.

Acknowledgements

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Conflict of interest

The authors declare that they have no conflict of interest.

Biographies

Jiatong Hu received her master's degree from the School of Information Science and Technology, University of Science and Technology of China, under the supervision of Prof. Ji Liu. Her research mainly focused on the association study of bone metabolism in type 2 diabetes using machine learning techniques, as well as investigating the gender differences in type 2 diabetes.

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