ORIGINAL RESEARCH

The Relationship Between GNRI Changes and Bone Metabolism Parameters and the Occurrence of Osteoporosis in Elderly Male Patients with T2D

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ABSTRACT

Background • Type 2 diabetes (T2D) and osteoporosis are both diseases with a high clinical incidence. Among the population with diabetes, T2D accounts for approximately 90%. With the change in people's eating habits and lifestyles, the incidence rate is gradually increasing.

Aim • We aimed to explore the relationship between the change in the Geriatric Nutritional Risk Index (GNRI) and the change in bone metabolism index parameters in elderly male patients with T2D and the occurrence of osteoporosis.

Methods • A total of 290 elderly male patients with type 2 diabetes (T2D) diagnosed in North China University of Science and Technology Affiliated Hospital from October 2019 to February 2022 were selected for GNRI evaluation. Of these patients, 148 with a GNRI > 98 (the normal group) and 142 with a GNRI ≤ 98 (the risk group) were selected for the study. The levels of 1,25-hydroxyvitamin D3 [1,25 (OH) 2D3], type 1 collagen N-terminal propeptide (P1NP), serum type 1 collagen C-terminal peptide hinge (S-CTX), osteocalcin (OC) and serum bone alkaline phosphatase (BALP) in the 2 groups were detected and compared. A dual-energy bone mineral density instrument was used to detect the bone mineral density (BMD) in the 2 groups. The logistic regression model was used to analyze the relationship between the occurrence of osteoporosis and indicators such as GNRI, and the receiver operating characteristic (ROC) curve was drawn to analyze the value of GNRI in predicting osteoporosis in elderly patients with T2D.

Results • The 1,25(OH)2D3 and P1NP levels in the risk group were lower than in the normal group, and the serum S-CTX and BALP levels in the risk group were higher than in the normal group; the differences were statistically significant (P <.05). The average BMD values of femoral neck, femur trochanter, Ward triangle and lumbar spine in the risk group were lower than in the normal group; the differences were statistically significant (P < .05). There were 70 patients with osteoporosis in the risk group and 9 patients with osteoporosis in the normal group. The difference in the detection rate of osteoporosis between the 2 groups was statistically significant ($\chi^2 = 68.281$; $P = .000 < .05$). The area under the curve (AUC) value under the ROC curve predicted by the GNRI for osteoporosis in elderly patients with T2D was 0.719, the sensitivity was 51.43% and the specificity was 97.26%. The logistic regression model showed that duration of diabetes, glycated hemoglobin A_{1c} (HbA_{1c}), S-CTX and BALP were independent risk factors for osteoporosis in elderly male patients with T2D (P < .05). Increased 1,25(OH)2D3, ALB and GNRI can reduce the risk for osteoporosis in elderly male patients with T2D (P < .05).

Conclusion • GNRI can reflect the nutritional status of elderly male patients with T2D, which is related to some extent to osteoporosis caused by loss of bone mass. (*Altern Ther Health Med.* 2023;29(1):85-89).

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INTRODUCTION

Type 2 diabetes (T2D) and osteoporosis are diseases with a high clinical incidence, and the incidence is gradually increasing.[1-2] Patients with T2D have a high risk for osteoporosis due to long-term hyperglycemia, relative lack of

insulin and changes in hormones.[3-4] Clinically, the change in bone mineral density (BMD) is an important basis for the diagnosis of osteoporosis, and the BMD can reflect the bone content of the body. Osteoporosis is a disease characterized by abnormal bone metabolism and bone loss. The changes in bone metabolism indices can evaluate the occurrence and development of osteoporosis, and can also reflect bone repair after treatment.[5] The number of patients with diabetes in China has been increasing, especially in the elderly population. Studies have shown that malnutrition can also lead to osteoporosis, and the nutritional status of patients with T2D is affected by many factors.[6-7] The Elderly Nutritional Risk Index (GNRI) is a tool for predicting the risk of morbidity and mortality in hospitalized elderly patients, and has been used to evaluate the prognosis of patients with suppurative liver abscess and hip fracture.[8] However, there are few studies on the relationship between GNRI and osteoporosis in elderly male patients with T2D, and the relationship between bone metabolic markers and GNRI in elderly male patients with T2D have not been fully elucidated.[9] This study will explore these issues and provide a basis for clinical diagnosis and treatment.

MATERIALS AND METHODS

General Information

A total of 290 elderly male patients with T2D diagnosed in North China University of Science and Technology Affiliated Hospital from October 2019 to February 2022 were selected for GNRI evaluation. Of these, 148 patients (the normal group) had a GNRI > 98, and 142 patients (the risk group) had a GNRI ≤ 98. The normal group consisted of 76 males and 72 females, average age 70.91 ± 3.89 years; the risk group consisted of 73 males and 69 females, average age 71.24 ± 4.01 years. The gender and age were not significantly different in the 2 groups.

Inclusion criteria. (1) Patients were age 65 to 85 years; (2) diagnostic criteria used for T2D were according to the 2018 American Diabetes Association (ADA) guidelines for diabetes diagnosis and treatment[10]; (3) diagnostic criteria for osteoporosis were from the *Guidelines for the Use of Bone Metabolic Markers in the Diagnosis and Treatment of Osteoporosis* (2012 edition)[11]; (4) the research program met the requirements of the medical ethics expert group in our hospital (No. S2019-230-04) and the patients and their families signed an informed consent form.

Exclusion criteria. (1) Cancer patients; (2) patients who had used calcium in the past month and bone metabolism drugs; (3) patients with thyroid disease; (4) patients with immune system diseases; (5) patients with tuberculosis and HIV infection; (6) patients with Cushing syndrome, rheumatoid arthritis, etc; (7) patients with chronic kidney disease, chronic liver disease, etc.

Instruments

A dual energy bone mineral density instrument (DiscoveryA, Hologic Company, Marlborough, Massachusetts, USA), and an enzymometer (Thermo Fisher Scientific, Waltham, Massachusetts, USA) were used in this study.

Bone Density Determination Methods

The instrument used was a dual-energy bone mineral density instrument (the accuracy was more than 99%, and the coefficient of variation was 0.25%), and the X-ray absorption method (DXA, Osteocore Type 3; Medilink, Gallargues-le-Montueux, France) was selected for the evaluation. The bone mineral density (BMD) of lumbar L1-L4, femoral neck, ward triangle, great trochanter and total hip were measured by 2 experienced physicians. The presence of osteoporosis was determined according to the *Guidelines for the Use of Bone Metabolism Markers in the Diagnosis and Treatment of Osteoporosis* (2012 Edition)[11] criteria.

Determination of Laboratory Indicators

3 mL fasting venous blood was collected in the morning and stored in a low temperature refrigerator. The supernatant was separated by centrifuge (1000 r/min for 15 min). The electrochemiluminescence method was used to determine the levels of total type I collagen amino-terminal protracted peptide (PINP), serum type 1 collagen C-terminal peptide hinge (S-CTX), osteocalcin (OC) and serum bone alkaline phosphatase (BALP).

The level of 1,25-hydroxyvitamin D3 (1,25(OH)2D3) was detected by ELISA. In accordance with the kit instructions, the standard solution was prepared first, and the absorbance value of the standard at 450 nm of the microplate reader (Thermo Fisher, USA) at each concentration was detected. The standard curve was plotted with the standard concentration as the abscissa and the absorbance value as the ordinate. After the sample to be tested was further treated, 3 parallel holes were set for each sample, and the absorbance value of each hole was detected under the same conditions as the standard sample. The average value was taken as the final result, and the absorbance value of the sample was substituted into the standard curve to obtain the concentration of the sample to be tested.

The blood samples of patients were collected according to the above methods, and fasting blood glucose (FBG), fasting insulin (FIns), albumin (ALB) and serum albumin were measured by Beckman AU5800 automatic biochemical analyzer (Beckman-Coulter, Brea, California USA). High pressure liquid chromatography was used to determine glycosylated hemoglobin (HbA_{1C}). HOMA-IR=FBG × FIns/22.5; the result was accurate to 0.01.

Ideal weight (male)=height−100−[(height−150)/4]. If the weight exceeded the ideal weight, weight/ideal weight=1. GNRI=(1.489×albumin (g/L)+41.7×[body weight/ideal body weight]. The study patients were divided into the normal GNRI group (GNRI > 98; n = 169) and the decreased GNRI group (GNRI ≤ 98; n = 47).[12]

Table 1. Comparison of Bone Metabolism Indices in the Risk and Normal Groups ($\overline{x} \pm s$)

Group	n	1,25(OH)2D3 (ng/mL)	P1NP (ng/mL)	S-CTX (ng/mL)	OC (ng/mL)	BALP (U/L)
Risk	142	17.84 ± 3.10	14.83 ± 2.54	1.64 ± 0.39	12.43 ± 2.67	76.58 ± 9.86
Normal	148	20.58 ± 3.76	17.33 ± 3.96	1.33 ± 0.25	11.97 ± 2.50	63.24 ± 7.76
t		-6.756	-6.370	8.092	1.515	12.831
P value		.000	.000	.000	.131	.000

Abbreviations: 1,25(OH)2D3, 1,25-hydroxyvitamin D3; BALP, serum bone alkaline phosphatase; OC, osteocalcin; P1NP, type I collagen amino-terminal protracted peptide; S-CTX, serum type 1 collagen C-terminal peptide hinge.

Statistical Processing

The measurement values of 1,25(OH)2D3, P1NP, S-CTX, BALP and other measurement indices in the study patients were tested by normal distribution, and were in accordance with the approximate normal or normal distribution, expressed as ($\overline{x} \pm s$), and compared in the 2 groups by *t* test. The χ^2 test was used for comparison between groups of non-grade counting data; the receiving operator characteristics (ROC) curve was plotted and the area under the curve (AUC) value was calculated; logistic regression analysis was used for multivariate analysis; IBM。 SPSS 21.0 software was used for data processing; test level α = .05.

RESULTS

Comparison of Bone Metabolism Indices in the 2 Groups

The 1,25(OH)2D3 and P1NP levels in the risk group were lower than in the normal group, and the serum S-CTX and BALP levels in the risk group were higher than in the normal group; differences were statistically significant ($P < .05$); see Table 1.

Comparison of BMD Values in the 2 Groups

The average BMD values of femoral neck, femur trochanter, Ward triangle and lumbar spine in the risk group were lower than in the normal group, and the differences were statistically significant ($P < .05$); Table 2.

The Value of GNRI in Predicting Osteoporosis in Elderly Patients with T2D

There were 70 patients with osteoporosis in the risk group and 9 patients with osteoporosis in the normal group. The difference in the detection rate of osteoporosis in the 2 groups was statistically significant ($\chi^2 = 68.281$; $P = .000 < .05$). The AUC value under the ROC curve predicted by GNRI for osteoporosis in elderly patients with T2D was 0.719, sensitivity was 51.43% and specificity was 97.26%. See Figure 1.

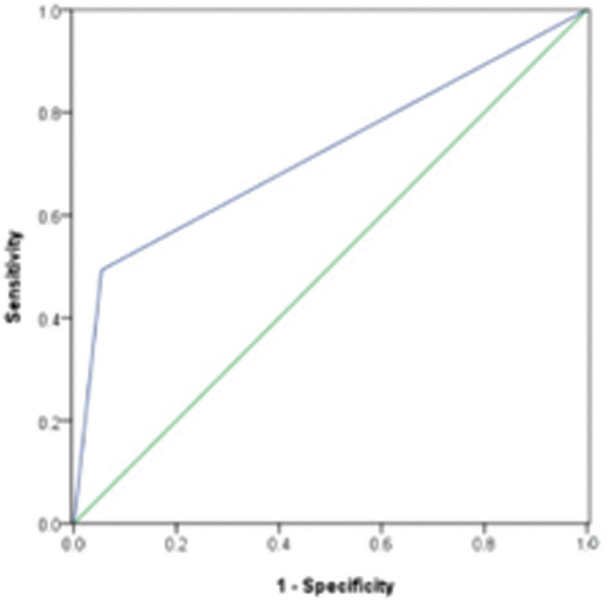
Univariate Analysis of Osteoporosis

The baseline data in the osteoporosis group and the normal bone mass group were compared. The results showed that the duration of diabetes, HbA_{1c} value, serum S-CTX and BALP levels in the osteoporosis group were higher than in the normal bone mass group. The 1,25(OH)2D3 and P1NP values in the osteoporosis group were lower than in the normal bone mass group, and the difference was statistically significant ($P < .05$); see Table 3.

Table 2. Comparison of Bone Mineral Density Values in the Risk and Normal Groups ($\overline{x} \pm s$)

Group	n	Femoral neck	Greater trochanter of femur	Ward's triangle	Lumbar spine
Risk	142	0.84 ± 0.14	0.81 ± 0.12	0.70 ± 0.10	0.95 ± 0.17
Normal	148	0.92 ± 0.16	0.94 ± 0.15	0.82 ± 0.16	1.03 ± 0.25
t		4.524	-8.129	-7.622	-3.174
P value		.000	.000	.000	.002

Figure 1. ROC curve of GNRI in predicting osteoporosis in elderly patients with T2D



Abbreviations: GNRI, Geriatric Nutritional Risk Index; ROC, receiver operating characteristics.

Multivariate Analysis of Osteoporosis

The occurrence of osteoporosis in elderly male patients with T2D was taken as the dependent variable, and the course of diabetes, HbA_{1c} value, serum S-CTX, BALP, 1,25(OH)2D3, P1NP and GNRI values with statistical significance in single factor analysis were taken as independent variables to establish the logistic regression model. The results showed that the

Table 3. Univariate Analysis of Osteoporosis in the Risk and Normal Groups

Factor	Osteoporosis group (n = 79)	Normal group (n = 211)	t/χ^2	*P* value
Age (years)	71.43 ± 4.03	70.72 ± 4.00	1.343	.180
BMI (kg/m^2)	24.72 ± 1.64	24.56 ± 1.51	0.784	.433
Duration of diabetes (years)	11.64 ± 2.75	10.33 ± 2.82	3.546	.000
HbA1c (%)	8.47 ± 0.96	8.10 ± 0.89	3.084	.002
FBG (mmol/L)	8.98 ± 0.86	8.81 ± 0.90	1.449	.148
FIns (μmol/mL)	12.74 ± 2.00	12.48 ± 1.92	1.015	.311
HOMA-IR	4.48 ± 0.87	4.31 ± 0.90	1.445	.150
ALB (g/L)	39.46 ± 2.24	40.72 ± 2.45	-3.989	.000
Hb (g/L)	130.5 ± 6.5	131.8 ± 5.8	1.643	.101
Smoking (%)	34 (43.04)	78 (36.97)	0.894	.344
Drinking (%)	36 (45.57)	103 (48.82)	0.243	.622
Hypertension (%)	36 (45.57)	107 (50.71)	0.608	.436
Hyperlipidemia (%)	42 (53.16)	98 (46.45)	1.039	.308
Coronary heart disease (%)	11 (13.92)	24 (11.37)	0.352	.553
1,25(OH)(2D3) (ng/mL)	17.71 ± 3.32	19.81 ± 3.51	-4.602	.000
P1NP (ng/mL)	14.67 ± 2.54	16.64 ± 3.54	-4.527	.000
S-CTX (ng/mL)	1.70±0.32	1.40 ± 0.31	7.273	.000
OC (ng/mL)	12.51±2.43	12.08 ± 2.56	1.291	.198
BALP (U/L)	78.04±8.87	66.68 ± 7.83	10.600	.000

Abbreviations: 1,25(OH)2D3, 1,25-hydroxyvitamin D3; ALB, albumin; BALP, bone alkaline phosphatase; BMI, body mass index; FBG, fasting blood glucose; FIns, fasting insulin; Hb, hemoglobin; HbA_{1c}, glycated hemoglobin; HOMA-IR, homeostatic model assessment for insulin resistance; P1NP, type 1 collagen N-peptide; OC, osteocalcin; S-CTX, serum type 1 collagen C-terminal peptide hinge.

Table 4. Logistic Regression Model Results

Index	β	SE	Walds	*P* value	OR	95% CI
Diabetes course	0.704	0.314	5.027	.032	2.022	1.093 to 3.741
HbA_{1c}	0.558	0.237	5.543	.021	1.747	1.098 to 2.780
ALB	-0.613	0.244	6.312	.003	0.542	0.336 to 0.874
1,25(OH)2D3	-0.482	0.221	4.757	.041	0.618	0.400 to 0.952
P1NP	-0.391	0.268	2.129	.184	0.676	0.400 to 1.144
S-CTX	0.771	0.304	6.432	.001	2.162	1.191 to 3.923
BALP	0.692	0.277	6.241	.004	1.998	1.161 to 3.438
GNRI	-0.815	0.302	7.283	.000	0.443	0.245 to 0.800
Constant term	1.333	0.784	2.891	.101	3.792	0.816 to 17.631

Abbreviations: 1,25(OH)2D3, 1,25-hydroxyvitamin D3; ALB, albumin; BALP, bone alkaline phosphatase; GNRI, Geriatric Nutritional Risk Index; HbA_{1c}, glycated hemoglobin; P1NP, type 1 collagen N-peptide; S-CTX, serum type 1 collagen C-terminal peptide hinge. β, regression coefficient; SE, standard error; Walds, Walds chi-square; OR, odds ratio; 95%CI, 95% confidence interval.

prolongation of diabetes course, increase in HbA_{1c} value, increase in S-CTX and increase in BALP were independent risk factors for osteoporosis in elderly male patients with T2D ($P < .05$). Increased 1,25(OH)2D3, ALB and GNRI can reduce the risk for osteoporosis in elderly male patients with T2D ($P < .05$); see Table 4.

DISCUSSION

Patients with T2D, especially older patients with metabolic disorder and insulin resistance, cannot use glucose normally, making fat and increasing protein decomposition, and thus usually have malnutrition. Osteoporosis often occurs in postmenopausal women and elderly men.[13] According to research,[14] the incidence of osteoporosis in older patients with T2D is significantly higher than in younger patients. Aging can affect the body' s bone remodeling process, resulting in bone remodeling imbalance, increasing the ratio of bone resorption and bone formation and resulting in bone loss. Second, the decrease in immune system activity in elderly patients affects a series of physiological functions and also promotes the occurrence of osteoporosis.

Type I collagen constitutes 90% of the bone matrix. PINP is produced by collagen cells during metabolism, and the PINP level can reflect the degree of synthesis and transformation of type I collagen. Bone metabolism can also be evaluated by the PINP level.[15] S-CTX, the decomposition product of type I collagen during bone resorption, can reflect bone resorption. PINP and S-CTX are more sensitive than other bone metabolic markers and are widely used in clinic.[16] The BMD can reflect the bone mass of the body during a certain period of time, and the bone metabolism index can reflect bone metabolism in the short term. Therefore, the selected bone metabolism index can better predict the risk for osteoporosis.

ALB and pre-ALB levels can reflect the nutritional status of the body; when inflammation, liver cirrhosis and malignant tumors are present, the levels are significantly reduced.[17-18] In addition, anemia and body mass index (BMI) are nutritional status indicators, so we also analyzed the hemoglobin (Hb) and BMI.

Nutritional risk can induce osteoporosis. The results of our study showed that the levels of 1,25(OH)2D3 and P1NP in the risk group were significantly lower than in the normal group, and the levels of serum S-CTX and BALP in the risk group were significantly higher than in the normal group. In addition, the average BMD values of femoral neck, femur trochanter, Ward triangle and lumbar spine in the risk group were significantly lower than in the normal group. Previous studies have shown that in the general population, Hb level and anemia status are related to BMD abnormality and fracture risk. In our study, we found that the difference in Hb and BMI in patients with or without T2D was not statistically significant, which may be related to the deviation of our selected samples. The BMD in patients with T2D with poor glycemic control had decreased more. The reason is that if the glucose level in collagen is high, a large number of glycosylation end products will be produced, which will affect bone strength,

induce apoptosis of bone cells and lead to abnormal bone growth. On the other hand, patients with T2D have insufficient insulin, and insufficient insulin synthesis and metabolism lead to diabetic bone loss. The GNRI includes multiple objective indicators such as ALB, body mass and ideal body mass, which are highly correlated with BMD. In this study, the number of patients with osteoporosis in the risk and normal groups was significantly different. High protein intake can effectively improve bone loss, maintain lower limb muscle function and prevent osteoporosis.

Our study results showed that the specificity of GNRI in predicting osteoporosis in elderly patients with T2D was high, but the sensitivity was poor. Prolonged duration of diabetes, and increased HbA_{1c}, S-CTX and BALP were independent risk factors for osteoporosis in elderly male patients with T2D. The increase in 1,25(OH)2D3, ALB and GNRI were protective factors.

At present, there is no unified standard for nutritional assessment. Hb and ALB have limitations when evaluated alone, and the assessment is not comprehensive enough. Clinically, multiple composite indicators are used. GNRI combines various indicators such as ALB, height and weight, which can objectively evaluate nutritional risk. An increase in 1,25(OH)2D3 is an independent protective factor for osteoporosis. The degree of oxidative stress in elderly patients with T2D is enhanced, osteoclasts are activated, bone resorption is promoted and BMD is reduced. 1,25(OH)2D3 is the active form of vitamin D, which can accelerate the absorption and reabsorption of calcium (Ca) and potassium (K) by the intestinal mucosa and renal tubules, respectively, and affect bone mineral metabolism and promote bone matrix mineralization. BMD measurement and nutritional risk assessment should be carried out as early as possible in elderly male patients with T2D, and timely intervention should be carried out according to the patient's particular situation to prevent the occurrence of osteoporosis and timely control of the disease.

Some studies have found that the GNRI score is positively correlated with BMD in patients with systolic heart failure. Low levels of GNRI were also found to be a risk factor for osteoporosis in male patients with rheumatoid arthritis.[19-20] Senile osteoporosis is characterized by decreased BMD and increased bone resorption. Based on previous studies, this study explored the relationship between osteoporosis and nutritional status in elderly male patients with T2D, and we found that increased 1,25(OH)2D3, ALB and GNRI could reduce the risk for osteoporosis in these patients.

In clinical work, we should emphasize the intervention of the above parameters, actively carry out health education to prevent osteoporosis and understand the indicators and methods for predicting the occurrence of osteoporosis, which is conducive to improving the prognosis in elderly patients.

Study Limitations

The results of our study were clinically significant; but there were also some study limitations. This was a retrospective study with limited sample size, leading to inevitable biases. Thus, the results of this study need to be confirmed by further studies.

CONCLUSION

In summary, the GNRI can reflect nutritional status in elderly male patients with T2D, which is related to osteoporosis caused by bone loss to some extent.

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