Association of geriatric nutritional risk index with bone mineral density and osteoporosis in postmenopausal elderly women with T2DM

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ABSTRACT

Background and Objectives: To investigate the relationship between geriatric nutritional risk index (GNRI) and osteoporosis (OP) in postmenopausal elderly women with type 2 diabetes mellitus (T2DM). **Methods and Study Design:** A total of 141 postmenopausal elderly women with T2DM was divided into OP and normal bone mineral density (BMD) groups, the differences in GRNI levels between the two groups were compared. According to the tertile levels of GRNI, T2DM were divided into three groups (T_1, T_2, T_3 groups), and the differences in OP prevalence and levels of BMD among the three groups were compared. **Results:** Among postmenopausal elderly women with T2DM, GNRI levels were lower in the OP group compared to the normal BMD group [(103.00±5.46) vs. (104.99±5.46), p<0.05)]. With elevated GNRI levels, the BMD levels of femoral, total hip, total body, and lumbar vertebrae (L) were gradually increased, which were higher in the T_3 group than in the T_1 group (all p< 0.05). GNRI levels were positively correlated with the BMD levels of femoral, spine, total hip, total body, L_1, L_2, L_3, L_4, and L_1-L_4. GNRI was an independent influencing factor for the occurrence of OP (OR=0.887, 95%CI [0.795,0.988]). The ROC curve showed that the GNRI combined with serum ALP and P levels had a high predictive value for OP, with an area under the curve of 0.725 (p<0.01). **Conclusions:** In postmenopausal elderly women with T2DM, GNRI was independently and positively correlated with BMD levels. GNRI may be a predictor development of OP.

Key Words: type 2 diabetes mellitus, geriatric nutritional risk index, postmenopausal women, osteoporosis, bone mineral density

INTRODUCTION

Osteoporosis (OP) is a systemic bone disease characterized by decreased bone mass and destruction of bone tissue microstructure.[1] According to the International Osteoporosis Foundation, OP affects 200 million women worldwide, with one-third of women and one-fifth of men over the age of 50 years experiencing an OP fracture in their lifetime. OP results in more than 8.9 million fractures annually, with OP fractures occurring every 3 seconds.[2] The global prevalence of OP is estimated to be 19.7%, with a higher prevalence in developing countries than in developed countries (22.1% vs.14.5%).[3] Approximately 10% of the world's population and more than 30% of postmenopausal women aged > 50 years develop OP.[4] In China, approximately 5.0% of men and 20.6% of women over 40 years of age have OP, while 10.5% of men and 9.7% of women over 40 years of age have OP fractures.[5] People with

diabetes are at a higher risk of developing OP, which has been estimated to occur in 7.29-53.71% of patients with type 2 diabetes mellitus (T2DM).[6] Therefore, early identification of the risk of OP in postmenopausal elderly women with T2DM is particularly important.

OP is considered as one of the complications of diabetes, that is, diabetes-induced bone fragility. The underlying mechanisms of diabetes-induced bone fragility are mainly due to the toxic effects of collagen cross-linking accumulation of advanced glycated end products in bone, impaired glucose metabolism, impairment of bone microvascular function and muscular endocrine function, oxidative stress, and lipid deposition, eventually result in reduced bone formation and bone remodeling.[7] In addition, the reduced insulin levels inhibit terminal differentiation of osteoblasts and mesenchymal stem cells, leading to low peak bone mass, which in turn promotes the onset and development of OP.[8]

The current gold standard for the diagnosis of OP relies on dual-energy X-ray absorptiometry (DXA) showing a femoral neck or lumbar spine T-score of $\leq$ -2.5.[1] GNRI, as an indicator to assess the nutritional status of older adults, has been used to assess the prognostic status of metabolic diseases such as heart disease,[9] sarcopenia,[10] diabetic retinopathy,[11] hypertension, hyperuricemia,[12] and other metabolic diseases. The GNRI is based on a combination of serum albumin and the ratio of actual to ideal body weight, which may be better to diagnose early malnutrition and the prognosis of related diseases. Malnutrition can lead to immunocompromise, exacerbating persistent low-grade inflammation and pro-inflammatory cytokine activation, which in turn directly stimulates bone resorption and reduces bone formation.[13]

On one hand, because of the higher incidence of osteoporosis in postmenopausal women, and on the other hand, the higher incidence of malnutrition in the elderly population. Currently, there are fewer studies on the relationship between GNRI and OP in the specific population of postmenopausal elderly women. Therefore, in this study, we investigated the relationships between GRNI, bone mineral density (BMD), and OP in postmenopausal elderly women with T2DM to provide prevention and treatment strategies for T2DM combined with OP in postmenopausal elderly women.

MATERIALS AND METHODS

Study subjects

A total of 141 postmenopausal elderly women with T2DM, who were hospitalized at the Department of Endocrinology of the First Hospital of Lanzhou University between January 2022 and April 2023, were selected for the study. The study was approved by the Ethics

Committee of the First Hospital of Lanzhou University and written informed consent was obtained from all participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (No.LDYYLL2023-409). The flow chart for subject' selection is shown Figure 1.

Inclusion criteria

The inclusion criteria were the following: (1) age ≥60 years; (2) patients meeting the 1999 World Health Organization (WHO) diagnostic criteria for T2DM based on medical history, symptoms, and laboratory tests; (3) duration of diabetes mellitus ≥1 year; and (4) T2DM patients with complete study data and information.

Exclusion criteria

The exclusion criteria were the following: (1) type 1 diabetes, gestational diabetes, or other special types of diabetes; (2) acute complications of diabetes such as diabetic ketoacidosis and diabetic hyperosmolar hyperglycemia; (3) patients with malignant tumors, immune disorders, acute infections, and thyroid and parathyroid disorders; (4) patients with severe heart failure, hepatic insufficiency [defined as aspartic acid aminotransaminase [AST]/alanine aminotransaminase [ALT] in whom levels were higher than three times the upper limit of normal], and renal insufficiency [estimated glomerular filtration rate (eGFR)<30mL/(min*1.73 m^2]; (5) patients who are bedridden for a long period of time; (6) patients treated with medications affecting calcium and phosphorus metabolism (e.g., thiazolidinediones, calcium supplements, vitamin D, diuretics, glucocorticoids, etc.) within 3 months; (7) non-menopausal women; and (8) patients with incomplete clinical data.

Collection of general characteristics of the study subjects

General patient information (age and sex), duration of diabetes, medication status, personal history, and any other disease history were collected from each participant, and the height, weight, and blood pressure were measured and recorded.

Body mass index (BMI)=Weight (kg)/Height(m^2)

Laboratory examinations

After fasting for 8 hours, 5 mL of venous blood was extracted from all subjects in the morning, from which serum was separated. Serum triglycerides (TG), total cholesterol (TC),

high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), uric acid (UA), alanine aminotransaminase (ALT), aspartic acid aminotransaminase (AST), fasting blood-glucose (FPG), albumin (Alb), alkaline phosphatase (ALP), calcium (Ca), and phosphorus (P). FPG, and post- challenge 2 -hour plasma glucose (2h-PG) levels were measured using a BS-220 automatic biochemical analyzer (Shenzhen Good Biological Company). Glycosylated hemoglobin (HbA1c) levels were determined using high-performance liquid chromatography (Bio-Rad-D10; Bio-Rad Laboratories). An electrochemiluminescence immunoassay (Roche Cobas-e801 Immunoassay Analyzer; Roche, Shanghai, China) was used to detect osteocalcin (OC), type I procollagen amino-terminal peptide (PINP), type I procollagen amino-terminal peptide (PINP), and β-Type I collagen carboxy-terminal peptide (β-CTX). 25-hydroxyvitamin D (25-(OH)VitD) was assayed by chemiluminescence (RT-6000 enzyme labeling analyzer, Shenzhen Radiometer Life Science Co. Ltd.). Meanwhile, fasting C-peptide (FCP) and fasting insulin (FINS) levels were determined using a chemiluminescence immunoassay (CENTAUR-XP automated chemiluminescence immunoanalyzer; Siemens Healthineers).

The reference value range for serum albumin is 40-55 g/L, with an inter-batch variability $<5\%$ and an intra-batch variability $\leq 4\%$.

An American GE dual-energy X-ray bone densitometer (Lunar iDXA) was used to detect the BMD values of different parts of the body (femoral, spine, total hip, total body, L_1, L_2, L_3, L_4, L_1-L_4) and their corresponding T- and Z-values, with the unit of BMD described as kg/cm^2. The assessed femoral regions included total femur, femur neck, trochanter, and intertrochanter.

Homeostatic model assessment of insulin resistance index (HOMA-IR)=FPG (mmol/L)× INS (mU/L)/22.5

Geriatric Nutrition Risk Index (GNRI) = [1.489 × serum albumin (g/L)] + [41.7 × (current weight/ideal weight (kg))].[14]

Women: Ideal weight = Height (cm) - 100 - [(Height (cm) - 150)/2.5], and when the actual weight exceeds the ideal weight, set actual weight/ideal weight = 1.

The estimated glomerular filtration rate (eGFR) was calculated using the Modified Diet in Renal Disease equation.[15]

eGFR (mL/min/1.73 m^2) = 186×Scr (mg/dL) – 1.154×age(years) – 0.203×0.742 (if women)×1.233 (if Chinese)

Diagnostic criteria

T2DM was diagnosed according to the 1999 WHO criteria for diabetes mellitus symptoms, with typical symptoms including polydipsia, polyuria, and unexplained weight loss, plus one of the following 3 items: (1) random blood glucose (refers to blood glucose at any time of the day) ≥11.1 mmol/L; (2) FPG ≥7.0 mmol/L; and (3) 2h-PG ≥11.1 mmol/L.

Osteoporosis was diagnosed according to the 1994 World Health Organization recommended diagnostic criteria for osteoporosis based on DXA bone mineral density: for postmenopausal women and men aged 50 years and older, when the T-value is ≥ -1.0, it suggests a normal bone mass; when -2.5< T-value < -1.0, it suggests a lower bone mass; and when the T-value is ≤ -2.5, it suggests osteoporosis.[16]

Study population grouping

According to the WHO-recommended diagnostic criteria for osteoporosis, postmenopausal elderly women with T2DM were divided into an osteoporosis (OP) group and a normal BMD group.

According to the tertile levels of GRNI, postmenopausal elderly women T2DM patients were divided into T_1(GNRI<102.45), T_2 (102.45≤GNRI<106.62), and T_3 groups (GNR I≥106.62).

Statistical analysis

All data were analyzed using the IBM SPSS 26,0 statistics software. Normally distributed measurement data were expressed as means±standard deviations ($\bar{x}$±s), and the difference between the groups were analyzed by independent samples t-test or one-way analysis of variance (ANOVA). The comparison between the two groups was analyzed based on whether equal variances were satisfied using Bonferroni's and Tamhane's tests. Non-normally distributed measures were expressed as medians (p25, p75), the difference between the groups was performed using Kruskal-Wallis non-parametric tests for independent samples. The enumeration data were expressed as frequencies and percentages (%), and differences among groups were compared using the Chi-square test. Pearson's or Spearman's correlation analysis was used to analyze the correlation between the GNRI and BMD levels at different sites, as well as clinical indicators. The independent correlation between GNRI and BMD at different sites in postmenopausal elderly women with T2DM was evaluated using multiple linear and binary logistic regressions. The predictive value of the GNRI combined with related indices

for OP was evaluated using the receiver operating characteristic curve (ROC). $p<0.05$ indicates statistical significance.

RESULTS

Comparison of the difference in GNRI levels and other indicators between the normal BMD and the OP groups in postmenopausal elderly women with T2DM

Among postmenopausal elderly women with T2DM, GNRI levels were significantly lower in the OP group than in the normal BMD group ($p<0.05$). In addition, BMI, FINS, P, and BMD levels (femoral, spine, total hip, total body, L_1, L_2, L_3, L_4, and L_1-L_4) were significantly lower in the OP group than in the normal BMD group (all $p<0.05$). However, ALP, OC, PINP, and β-CTX levels were higher than those in the normal BMD group (all $p<0.05$). The other indicators were not significantly different between the two groups ($p>0.05$) (Table 1)

Comparison of the prevalence of OP and BMD levels at different GNRI level groups in postmenopausal elderly women with T2DM

According to GNRI tertiles, postmenopausal elderly women with T2DM were divided into three groups. The results showed that the prevalence of OP in the T_3 group (27.9%) was lower than that in the T_1 and T_2 groups (43.0% and 29.1%, both p>0.05), but the difference was not statistically significant. (Figure 2)

With elevated GNRI levels, the BMD levels of femoral, total hip, total body, and lumbar vertebrae (L) were gradually increased, which were higher in the T_3 group than in the T_1 group (all $p< 0.05$). The BMD levels of the spine, L_2, L_3, L_4, and L_1-L_4 were not significantly different among the three groups ($p>0.05$). (Figure 2)

Correlation between GNRI and various clinical indicators in postmenopausal elderly women with T2DM

The GNRI positively correlated with BMI, Alb, ALP, UA, ALT, TG, Ca, and OC (all $p<0.05$) and negatively correlated with age ($p<0.05$). There were no correlations between GNRI and duration of diabetes, HbA1c, FCP, 25-(OH)VitD, FPG, FINS, HOMA-IR, AST, TC, HDL-C, LDL-C, P, PINP, β-CTX. (Table 2)

Correlation between GNRI and BMD levels in postmenopausal elderly women with T2DM

In postmenopausal elderly women with T2DM, GNRI was significantly and positively correlated with femoral, spine, total hip, total body, L1, L2, L3, L4, and L1-L4 BMD levels (r=0.265,0.182,0.267, 0.260, 0.244, 0.235,0.204, 0.183, and 0.224, all $p<0.05$). (Figure 3)

Multiple linear regression analysis of the relationship between GNRI and BMD in postmenopausal elderly women with T2DM

Multiple linear regression analysis was performed with the BMD at different sites as the dependent variable and the GNRI as the independent variable. BMI and Alb were excluded from the modeling because of their covariance with the GNRI.

The GNRI was independently and positively correlated with the levels of the femoral, total hip, total body, L_1, and L_2 BMD (all $p<0.05$) when the variables were not adjusted in Model 1. Model 2 was further adjusted for age, AST, ALT, TC, TG, OC, PINP, β-CTX, 25-(OH)VitD, Ca, P, UA, and ALP on the basis of Model 1, GNRI remained independently and positively correlated with the levels of femoral, total hip, total body, L_1, and L_2 BMD (all $p<0.05$). (Table 3)

Binary logistic regression analysis of the relationship between OP and GNRI in postmenopausal women with T2DM patients

OP was the dependent variable; age, AST, ALT, ALP, UA, Ca, P, 25-(OH)VitD, dyslipidemia (1=Yes,0=No), hypertension (1=Yes,0=No), fatty liver disease (1=Yes,0=No), and GNRI were considered independent variables; and BMI and Alb were excluded from modeling because of their covariance with GNRI.

The results showed that GNRI was influencing factors for the occurrence of OP (OR=0.887, 95% CI [0.795, 0.988]). In addition, P and ALP levels were independent influencing factors for the occurrence of OP (OR=0.033, 95%CI [0.002,0.449] and OR=1.018, 95%CI [1.002,1.034]). No association was found between age, AST, ALT, UA, 25-(OH)VitD, Ca, dyslipidemia, hypertension, fatty liver disease, and the occurrence of OP (all $p>0.05$). (Table 4)

The predictive value of GNRI combined with other indicators for OP in postmenopausal elderly women with T2DM

Binary logistic analysis revealed that GNRI, ALP, and P levels were closely associated with the occurrence of OP. Based on this, an OP prediction model based on the combined

predictors was developed in this study, which is a composite predictor (L)=12.419+0.018*ALP-3.623*P-0.085*GNRI. The results of the ROC curve showed that the area under the curve, including ALP, P, and GNRI, for the prediction of OP was 0.725 (95%CI [0.640,0.810], p<0.01), with a sensitivity of 69.8% and specificity of 66.0%, suggesting a high predictive value of the combined indicators. (Figure 4)

DISCUSSION

With lifestyles changing and the population aging, the number of patients with T2DM and OP is increasing annually. OP is a systemic disease that mainly affects the elderly. It is relatively more prevalent among women, and particularly postmenopausal women. OP is usually accompanied by the loss of mobility, chronic pain, etc., which has a great impact on physical and mental health.[17] Diet and nutritional status are key to the management and treatment of T2DM. Patients with T2DM frequently exhibit disturbances in both glucose and lipid metabolism, along with insulin resistance (IR). These conditions often co-occur with other metabolic disorders such as impaired glucose utilization and increased fat and protein catabolism, leading to nutritional imbalances of varying degrees.[18] As we get older, the body composition associated with aging changes to some degree, with a decrease in muscle mass, bone, and water content and a relative increase in fat content. On the one hand, this change in body composition may lead to a decrease in insulin sensitivity, resulting in IR and exacerbation of nutritional imbalances; on the other hand, a decrease in muscle mass may result in a decrease in the protection of bones and joints, and a significant increase in the risk of falls and fractures.[19,20] Thus, nutrition, aging, IR, T2DM, and OP are intricately associated.

Nutrients, including micronutrients such as calcium, vitamin D, and phosphorus, are key bone components, and proteins are also an important bone nutritional component.[21] A reasonable dietary regimen and good nutritional status are key factors in preventing bone loss and OP.[22] The GNRI is a simple indicator for assessing the nutritional status of the elderly; it combines height, weight, and albumin to reflect the nutritional status of the body; it is easy to operate, highly reproducible, and convenient to carry out in the community and other primary health care organizations. In recent years, studies have shown a strong correlation between the GNRI and OP. For example, Wang J et al. showed that the GNRI was positively associated with femoral BMD and negatively associated with the risk of OP in a population of postmenopausal women in the United States.[23] However, few studies have investigated the relationship between GNRI, BMD, and OP in postmenopausal elderly women with T2DM.

In a cross-sectional study, Huang et al. showed that lower GNRI levels were a risk factor for the development of OP in older adults and could be used as a predictor of OP risk in older adults.[24] A cross-sectional study in China showed that in an elderly population, patients with higher GNRI levels had higher BMD and T-scores.[25] Similar to these results, our results also found a strong association between the GNRI and BMD as well as OP in postmenopausal elderly women with T2DM.

In this study on postmenopausal elderly women with T2DM, we found that the GNRI levels in the OP group was significantly lower than that in the normal BMD group. The prevalence of OP gradually decreased as the level of GNRI increased, and the level of BMD at different sites, such as the femoral, total hip, total body, and L_1, gradually increased, suggesting that patients with poorer nutritional status are at higher risk of OP. In addition, in this study, the GNRI was significantly and positively correlated with BMD at different sites, such as the femoral, spine, total hip, total body, L_1, L_2, L_3, L_4, and L_1-L_4. Multiple linear regression analysis suggested that GNRI was independently and positively associated with BMD levels at different sites such as femoral, total hip, total body, L_1, and L_2. These associations remained after adjusting for confounders such as AST, ALT, TC, TG, OC, PINP, β-CTX, 25-(OH)VitD, Ca, P, UA, and ALP. This is consistent with a cross-sectional study from northern China, which also indicated that GNRI was positively correlated with BMD levels of the lumbar spine, femoral neck, and hip in patients with T2DM.[26]

Ca intake and vitamin D status are essential for bone homeostasis. Malnutrition may cause some impairment of Ca and P absorption, leading to poor bone mineralization and promoting the development and progression of OP. The protein intake affects the production of insulin-like growth factor-1 (IGF-1), an important nutrient hormone that stimulates the growth of skeletal muscle, cartilage, and bone. It may also increase Ca and P absorption in the intestine through the synthesis of osteotriol and regulate Ca and P reabsorption in the kidneys, ultimately affecting bone mineralization.[27] With increasing age, the level of IGF-1 decreases. Lower IGF-1 expression can, in turn, decrease BMD levels and promote the occurrence of OP by affecting collagen fiber repair, the mechanical stress capacity of bone trabeculae, or the flow of interstitial components of bone cells.[28] Zhang et al. reported that in postmenopausal women patients, IGF-1 levels in the OP group were significantly lower than those in the normal BMD group, and IGF-1 was significantly and positively correlated with BMD levels in the lumbar spine as well as the left and right hip joints.[29] Qing et al. found that the GNRI remained significantly associated with the BMD of the lumbar spine and total hip in older men and women; however, no association between the GNRI and lumbar spine BMD was

found in multivariate linear regression after adjusting for confounding variables.[25] OP in the elderly most often affects the peripheral cortical bone. The vertebral body is composed primarily (approximately 80%) of trabecular bone, whereas the long bones and hip bones are composed primarily of cortical bone (80% and 40%, respectively), suggesting that malnutrition may have a relatively greater impact on cortical bone BMD in older women.[30]

Protein is an important nutrient for bone homeostasis. A study by Afshinnia F et al., which included a large US population, showed that hypoalbuminemia was independently associated with the risk of OP in the femoral neck, total hip, and lumbar spine.[31] Hypoproteinemia may be associated with nuclear factor-κB (NF-κB) as well as inflammatory cytokines (e.g., receptor activators of NF-κB ligands, TNF-α, bacterial endotoxin, Toll-like receptor ligands, or oxygen free radicals), which can lead to OP through activation of osteoclasts and inhibition of osteogenesis.[32] Adequate protein intake is essential for maintaining bone strength, and a higher protein intake may help reduce the risk of hip fractures by improving bone strength.[33] In addition, protein malnutrition may contribute to the development of sarcopenia, exacerbating muscle and bone loss and contributing to the onset and progression of OP. The reduction in muscle protein mass is the result of an imbalance between protein anabolism and catabolism. The anabolism is mainly triggered by the intracellular insulin signaling pathway and the IGF-1 receptor pathway (IGF-1/AKT/mTOR), whereas catabolism involves a number of specific protein hydrolysis pathways and is influenced by a variety of factors such as insufficient nutrient intake, lack of physical activity, hormone deficiencies, and pro-inflammatory cytokines.[34] Postmenopausal women or older women with sarcopenia had a greater risk of developing OP than those without sarcopenia, and the prevalence of OP increased progressively with increasing severity of sarcopenia.[35, 36]

Ji et al. reported a positive correlation between GNRI and both Ca and 25-(OH)VitD, and a negative correlation with PINP. However, they found no correlation with β-CTX.[26] In this study, we found a significant positive correlation between GNRI and ALP, Ca, and OC. However, we found no correlation between GNRI and the other bone metabolism-related indices such as 25-(OH)VitD, P, PINP, and β-CTX. The discrepancy in these findings might be attributed to the diminished estrogen secretion in postmenopausal women, which potentially affects the absorption and uptake of active 25-(OH)VitD, further influencing Ca and P assimilation. In addition, in malnourished patients, calcium and P metabolism is abnormal, which affects the levels of bone conversion markers.[37] In the binary logistic regression analysis, we determined that P and ALP are independent influencing factors for the occurrence of OP, and the ROC curve indicated that GNRI combined with P and ALP may be

considered as a predictor of the occurrence of OP in postmenopausal elderly women with T2DM. A cross-sectional study indicated a negative correlation between GNRI and ALP after adjusting for confounders in elderly T2DM patients in northern China.[26] Additionally, research indicates a reverse relationship between GNRI levels and serum ALP levels in women patients undergoing hemodialysis.38 It should be noted that while ALP is associated with bone growth and development, serving as an indicator of osteoblast maturation and activation, our study measured ALP levels originating from the liver, not bone alkaline phosphatase (BALP), which is a more direct indicator of bone metabolism. However, we still found that GNRI combined with P and ALP may better predict the occurrence of OP in postmenopausal elderly women with T2DM.

A Japanese multicenter prospective observational study showed that GNRI could be a simple predictor for assessing the prognosis of elderly patients with hip fractures.[39] In this study, GNRI is an independent protective factor for the occurrence of OP in postmenopausal elderly women with T2DM, which means the higher the GNRI, the lower the nutritional risk and the lower the risk of OP occurrence. Therefore, GNRI may serve as an important assessment tool for bone health in postmenopausal elderly women. Postmenopausal elderly women should undergo nutritional assessments and BMD measurements to intervene early and minimize the occurrence of OP and fractures.

The current study has some limitations. Firstly, this is a cross-sectional study, which cannot clearly draw a causal relationship between GNRI and OP, and further basic experiments and prospective cohort studies are needed to verify it. Secondly, all study populations were hospitalized patients with type 2 diabetes. Due to the complex and diverse hypoglycemic drugs used, we cannot rule out the influence of hypoglycemic drugs on the results. Thirdly, the effects of dietary habits and physical activities on OP were not considered. Finally, the study had a small sample size.

In conclusion, in postmenopausal elderly women with T2DM, the BMD gradually increased with the increase in GNRI levels, which was independently and positively correlated with BMD levels and was an independent influencing factor for the occurrence of OP. GNRI combined with serum P and ALP levels may be considered a predictor of OP in postmenopausal elderly women with T2DM.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

All authors declare that they have no competing interests.

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Table 1. Comparison of the differences in GNRI levels and other indicators between the normal bone mass group and the OP group in postmenopausal elderly women with T2DM

Index	Normal BMD (N=55)	OP (N=86)	*p*
Age (year)	68.05 ± 6.47	70.12 ± 6.28	0.061
Duration (year)	10.50(6.75,19.25)	12.00(7.00,18.25)	0.743
SBP (mmHg)	155.04 ± 22.13	153.84 ± 23.67	0.770
DBP (mmHg)	85.49 ± 17.81	84.35 ± 19.76	0.735
BMI (kg/m²)	25.02 ± 3.35	22.48 ± 2.98	<0.001
Alb (g/L)	42.76 ± 3.36	42.37 ± 3.02	0.474
HbA1c (%)	8.48 ± 2.06	8.31 ± 1.86	0.627
FPG (mmol/L)	8.71 ± 3.32	8.95 ± 2.92	0.660
FCP (mIU/L)	1.44 ± 0.90	1.28 ± 0.99	0.350
FINS (ng/mL)	8.36(5.71,14.08)	6.70(4.74,8.60)	0.023
HOMA-IR	3.31(2.00,5.18)	2.46(1.69,4.01)	0.062
AST (U/L)	19.00(16.00,23.00)	20.00(16.00,28.25)	0.450
ALT (U/L)	15.00(12.75,21.50)	18.00(13.00,25.00)	0.369
TC (mmol/L)	4.71 ± 1.07	4.40 ± 1.00	0.090
TG (mmol/L)	1.69(1.05,2.37)	1.39(1.06,1.79)	0.135
HDL-C (mmol/L)	1.15 ± 0.26	1.19 ± 0.27	0.404
LDL-C (mmol/L)	3.06 ± 0.78	2.85 ± 0.79	0.122
25-(OH)VitD (ng/mL)	11.85(8.45,16.90)	11.45(8.38,16.48)	0.909
UA (μmol/ L)	316.09 ± 70.50	295.99 ± 82.39	0.138
ALP (U/L)	68.65(61.58,80.68)	85.65(66.88,102.90)	0.018
Ca (mmol/L)	2.19 ± 0.11	2.20 ± 0.22	0.672
P (mmol/L)	1.30 ± 0.15	1.20 ± 0.16	0.001
OC (ng/mL)	12.54 ± 3.75	16.29 ± 6.86	0.001
PINP (ng/mL)	33.75(25.18,44.00)	44.15(35.10,60.23)	<0.001
β-CTX (pg/mL)	321.50(197.00,504.75)	490.00(285.00,700.50)	0.001
GRNI	104.99 ± 5.46	103.00 ± 5.46	0.045
BMD- femoral (g/cm²)	1.06 ± 0.08	0.85 ± 0.10	<0.001
BMD- spines (g/cm²)	1.09 ± 0.08	0.80 ± 0.08	<0.001
BMD- total hip(g/cm²)	0.89 ± 0.09	0.65 ± 0.08	<0.001
BMD- total body (g/cm²)	1.08 ± 0.08	0.84 ± 0.08	<0.001
BMD-L_1 (g/cm²)	1.03 ± 0.08	0.71 ± 0.08	<0.001
BMD-L_2 (g/cm²)	1.13 ± 0.09	0.75 ± 0.08	<0.001
BMD-L_3 (g/cm²)	1.22 ± 0.10	0.84 ± 0.15	<0.001
BMD-L_4 (g/cm²)	1.24 ± 0.13	0.87 ± 0.11	<0.001
BMD-L_1-L_4 (g/cm²)	1.16 ± 0.08	0.80 ± 0.08	<0.001
Hypertension (n, %)	41(74.5%)	64(74.4%)	0.987
Fatty liver disease (n, %)	19(34.5%)	24(27.9%)	0.404
Dyslipidemia (n, %)	26(47.3%)	33(38.4%)	0.296

SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; HbAlc: glycated hemoglobin; Alb: albumin; FPG: fasting blood-glucose; FCP: fasting C-peptide; FINS: fasting insulin; HOMA-IR: insulin resistance index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; 25-(OH)VitD: 25-hydroxyvitamin D; UA: uric acid;ALP: alkaline phosphatase; Ca: calcium; P: phosphorus; OC: osteocalcin; PINP: type I procollagen amino-terminal peptide;β-CTX: β-Type I collagen carboxy-terminal peptide; GRNI:geriatric nutritional risk index; BMD: bone mineral density; L: lumbar vertebrae. OP: osteoporosis

Table 2. Correlation between GNRI and various clinical indicators in postmenopausal elderly women with T2DM

	GNRI	
	r	*p*
Age (year)	-0.191	0.023
Duration (year)	-0.089	0.292
BMI (kg/m²)	0.433	<0.001
HbA1c (%)	-0.065	0.447
Alb (g/L)	0.914	<0.001
25-(OH)VitD (ng/mL)	-0.033	0.704
ALP (U/L)	0.228	0.007
UA (μmol/ L)	0.193	0.022
FPG (mmol/L)	0.025	0.775
FCP (mIU/L)	0.170	0.053
FINS (ng/mL)	0.098	0.266
HOMA-IR	0.091	0.298
AST (U/L)	0.105	0.217
ALT (U/L)	0.180	0.033
TC (mmol/L)	0.101	0.154
TG (mmol/L)	0.197	0.019
HDL-C (mmol/L)	-0.030	0.725
LDL-C (mmol/L)	0.142	0.093
Ca (mmol/L)	0.282	0.001
P (mmol/L)	0.148	0.081
OC (ng/mL)	0.182	0.008
PINP (ng/mL)	0.131	0.122
β-CTX (pg/mL)	0.154	0.068

SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; HbAlc: glycated hemoglobin; Alb: albumin; FPG: fasting blood-glucose; FCP: fasting C-peptide; FINS: fasting insulin; HOMA-IR: insulin resistance index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; 25-(OH)VitD: 25-hydroxyvitamin D; UA: uric acid;ALP: alkaline phosphatase; Ca: calcium; P: phosphorus; OC: osteocalcin; PINP: type I procollagen amino-terminal peptide;β-CTX: β-Type I collagen carboxy-terminal peptide.

Table 3. Multiple linear regression analysis of the relationship between GNRI and BMD in postmenopausal elderly women with T2DM

Index	β	t	*p*	95%CI
Model 1				
BMD-Femoral (g/cm²)	0.223	2.431	0.017	(0.001,0.010)
BMD- Spines (g/cm²)	0.132	1.418	0.159	(-0.002,0.009)
BMD- Total hip(g/cm²)	0.222	2.421	0.017	(0.001,0.010)
BMD- Total body (g/cm²)	0.215	2.340	0.021	(0.001,0.010)
BMD-L1 (g/cm²)	0.197	2.140	0.034	(0.000,0.012)
BMD-L2 (g/cm²)	0.185	2.005	0.047	(0.000,0.014)
BMD-L3 (g/cm²)	0.161	1.729	0.086	(-0.001,0.014)
BMD-L4 (g/cm²)	0.129	1.379	0.171	(-0.002,0.012)
BMD-L1-L4 (g/cm²)	0.174	1.882	0.062	(0.000,0.013)
Model 2				
BMD-Femoral (g/cm²)	0.234	2.552	0.012	(0.001,0.011)
BMD-Spines (g/cm²)	0.152	1.573	0.119	(-0.001,0.010)
BMD-Total hip (g/cm²)	0.232	2.528	0.013	(0.001,0.011)
BMD-Total body (g/cm²)	0.213	2.389	0.019	(0.001,0.010)
BMD-L1 (g/cm²)	0.196	2.069	0.041	(0.000,0.012)
BMD-L2 (g/cm²)	0.183	2.019	0.046	(0.000,0.014)
BMD-L3 (g/cm²)	0.147	1.444	0.152	(-0.002,0.015)
BMD-L4 (g/cm²)	0.105	0.987	0.326	(-0.004,0.012)
BMD-L1-L4 (g/cm²)	0.163	1.687	0.095	(-0.001,0.013)

AST: aspartate aminotransferase; ALT: alanine aminotransferase; TC: total cholesterol; TG: triglycerides; 25-(OH)VitD: 25-hydroxyvitamin D; UA: uric acid;ALP: alkaline phosphatase; Ca: calcium; P: phosphorus; OC: osteocalcin; PINP: type I procollagen amino-terminal peptide;β-CTX: β-Type I collagen carboxy-terminal peptide; BMD: bone mineral density; L: lumbar vertebrae. B: standardized regression coefficients; t: test statistics in the linear regression; CI: confidence interval
Model 1: Unadjusted variables; Model 2: Model 1Adjusted age; AST; ALT; TC; TG; OC; PINP; β-CTX; 25-(OH)VitD; Ca; P; UA; ALP.

Table 4. Binary logistic regression analysis of the relationship between OP and GNRI in postmenopausal women with T2DM patients

Index	B	*p*	OR	95%CI
Age (year)	0.032	0.363	1.032	(0.964,1.105)
AST(U/L)	-0.009	0.847	0.991	(0.904,1.087)
ALT(U/L)	0.027	0.405	1.027	(0.965,1.093)
25-(OH)VitD (ng/mL)	-0.001	0.977	0.999	(0.930,1.073)
ALP (U/L)	0.018	0.025	1.018	(1.002,1.034)
Ca (mmol/L)	0.430	0.673	1.537	(0.209,11.307)
P (mmol/L)	-3.046	0.010	0.033	(0.002,0.449)
UA (μmol/ L)	0.002	0.571	0.998	(0.993,1.004)
Dyslipidemia	-0.365	0.390	1.032	(0.964,1.105)
Hypertension	0.207	0.676	1.230	(0.465,3.253)
Fatty liver disease	0.040	0.928	1.041	(0.434,2.499)
GNRI	-0.120	0.030	0.887	(0.795,0.988)

AST: aspartate aminotransferase; ALT: alanine aminotransferase; 25-(OH)VitD: 25-hydroxyvitamin D; ALP: alkaline phosphatase; Ca: calcium; P: phosphorus; GRNI: geriatric nutritional risk index; B: regression coefficients; OR: odds ratio; CI: confidence interval

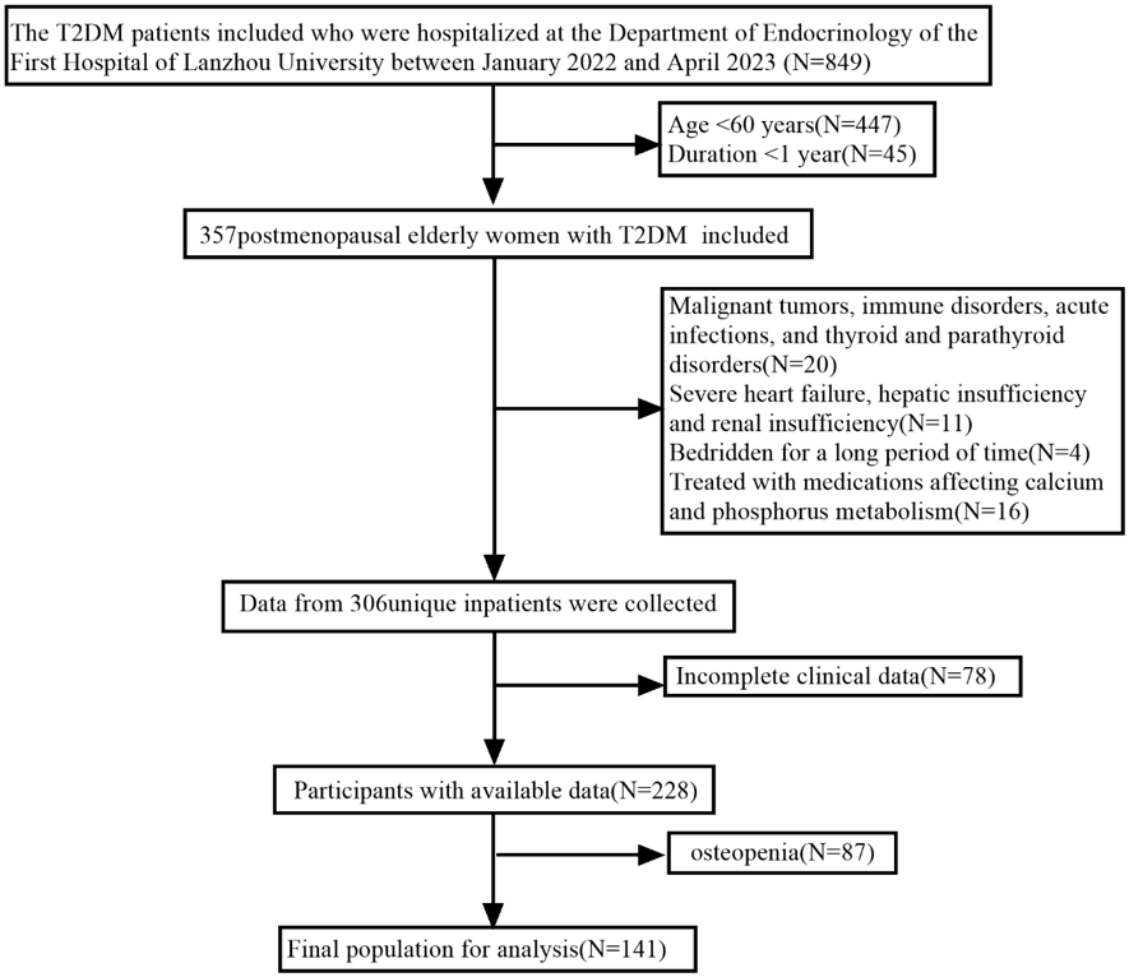

Figure 1. Flow chart for subject selection.

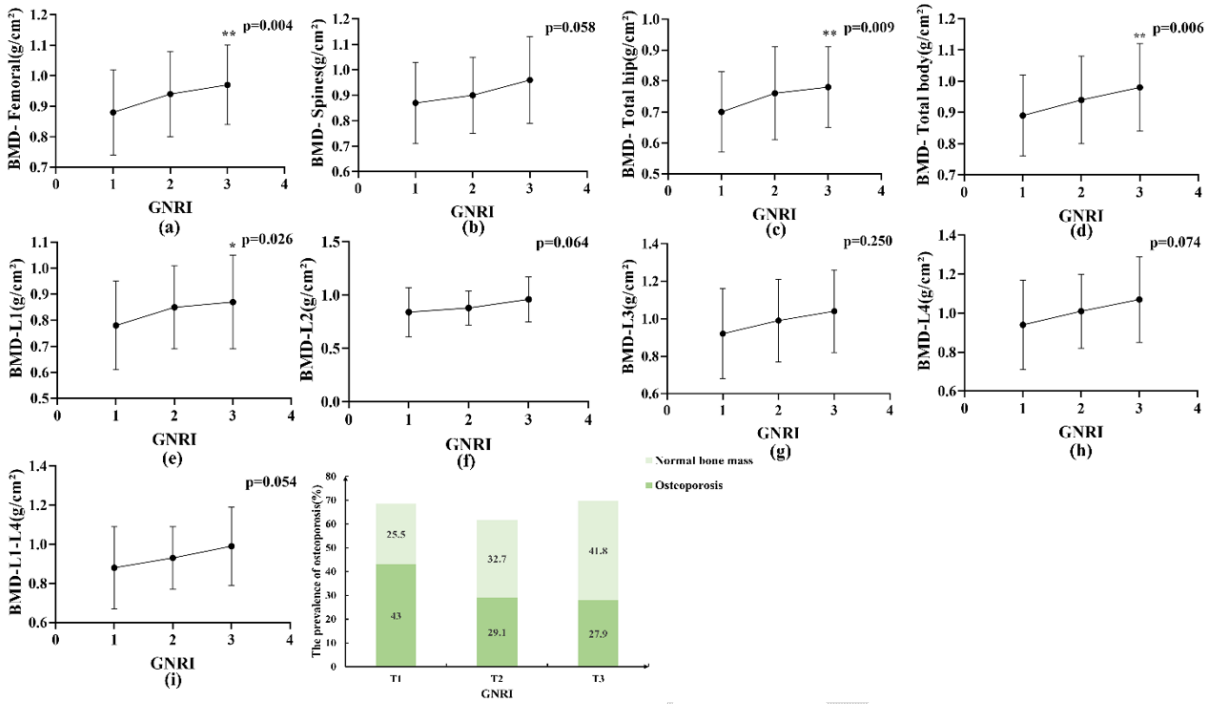

Figure 2. Comparison of the prevalence of OP and BMD levels at different GNRI level groups in postmenopausal elderly women with T2DM. **p*<0.05 when compared to T_1 group；# *p*<0.05 when compared to T_2 group

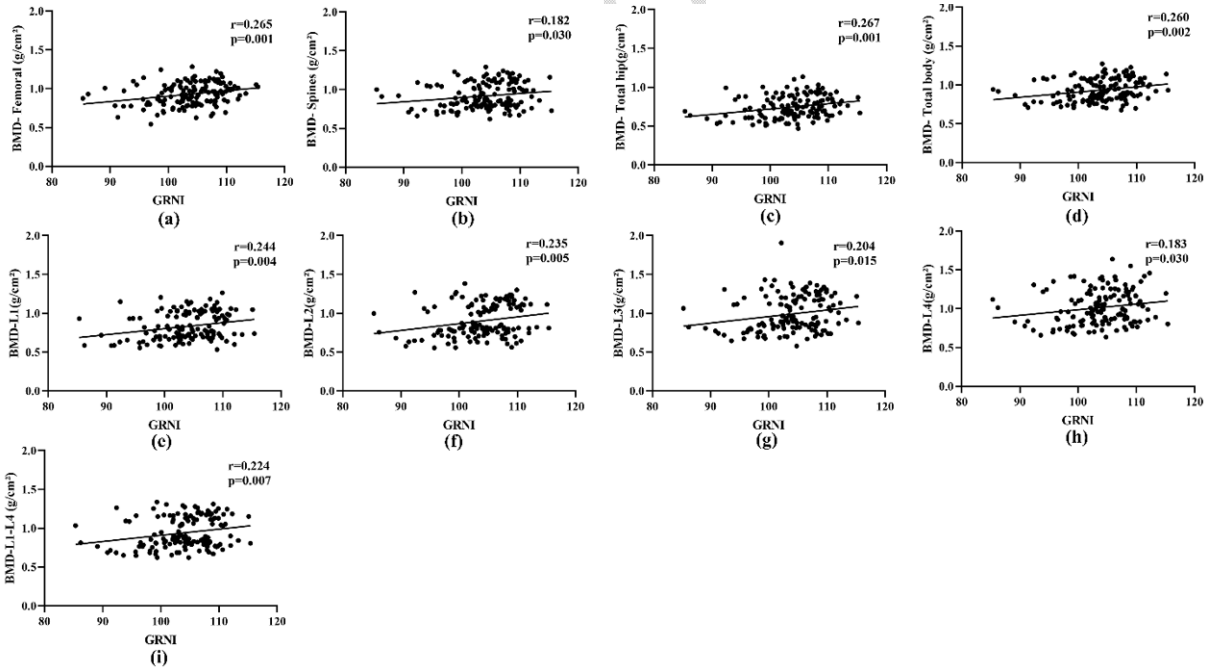

Figure 3. Correlation between GNRI and BMD levels in postmenopausal elderly women with T2DM. GRNI: geriatric nutritional risk index; BMD: bone mineral density; L: lumbar vertebrae

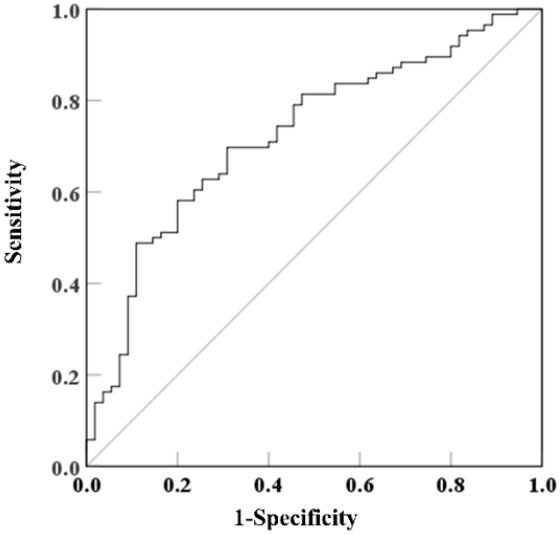

Figure 4. The predictive value of GNRI combined with other indicators for OP in postmenopausal elderly women with T2DM. ALP: alkaline phosphatase; P: phosphorus