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Case Control Study

Associations between Geriatric Nutrition Risk Index, bone mineral density and body composition in type 2 diabetes patients

Nutrition, bone mineral density and diabetes

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Abstract

BACKGROUND

Type 2 diabetes mellitus (T2DM), a fast-growing issue in public health, is one of the most common chronic metabolic disorders in older individuals. Osteoporosis and sarcopenia are highly prevalent in type 2 diabetes mellitus (T2DM) patients and may result in fractures and disabilities. In people with T2DM, the association between nutrition, sarcopenia, and osteoporosis has rarely been explored.

AIM

To evaluate the connections among nutrition, bone mineral density (BMD) and body composition in patients with T2DM.

METHODS

We enrolled 689 patients with T2DM for this cross-sectional study. All patients underwent dual energy X-ray absorptiometry (DXA) examination and were categorized according to baseline Geriatric Nutritional Risk Index (GNRI) values calculated from serum albumin levels and body weight. The GNRI was used to evaluate nutritional

status, and DXA was used to investigate BMD and body composition. Multivariate forward linear regression analysis was used to identify the factors associated with BMD and skeletal muscle mass index.

RESULTS

Of the total patients, 394 were men and 295 were women. Compared with patients in tertile 1, those in tertile 3 who had a high GNRI tended to be younger and had lower HbA1c, higher BMD at all bone sites, and higher appendicular skeletal muscle index (ASMI[Editor1]). These important trends persisted even when the patients were divided into younger and older subgroups. The GNRI was positively related to ASMI (men: r = 0.644 p< 0.001; women: r = 0.649 p< 0.001), T-FAT (men: r = 0.453 p< 0.001; women: r = 0.557 p< 0.001), BMD at all bone sites, LS-BMD (men: r = 0.110 P = 0.029; women: r = 0.256 p< 0.001), FN-BMD (men: r = 0.293 p< 0.001; women: r = 0.273 p< 0.001), and H-BMD (men: r = 0.358 p< 0.001; women: r = 0.377 p< 0.001). After adjustment for other clinical parameters, the GNRI was still significantly associated with BMD at the lumbar spine and femoral neck. Additionally, a low lean mass index and higher β-CTX were associated with low BMD at all bone sites. Age was negatively correlated with ASMI, whereas weight was positively correlated with ASMI.

CONCLUSION

Poor nutrition, as indicated by a low GNRI, was associated with low levels of AMSI and BMD at all bone sites in type 2 diabetes mellitus patients. Using the GNRI to evaluate nutritional status and using DXA to investigate body composition in patients with T2DM is of value in assessing bone health and physical performance.

Key Words: Geriatric Nutrition Risk Index; Bone mineral density; Skeletal muscle mass; Type 2 diabetes

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Core Tip: Osteoporosis and sarcopenia are highly prevalent in type 2 diabetes mellitus patients. In people with T2DM, the association between nutrition, sarcopenia, and osteoporosis has rarely been explored**.** We observed that poor nutrition, as indicated by a low GNRI, was associated with low levels of AMSI and BMD at all bone sites in type 2 diabetes mellitus patients. Using the GNRI to evaluate nutritional status and using DXA to investigate body composition in patients with T2DM is of value in assessing bone health and physical performance.

INTRODUCTION

Over the past few years, there has been a rise in the prevalence of osteoporosis and sarcopenia among the elderly population, leading to physical impairment, diminished quality of life and even death of patients[1, 2]. Type 2 diabetes mellitus (T2DM), a rapidly growing public health problem, is one of the most common chronic metabolic disorders in older individuals[3]. For patients with type 2 diabetes mellitus, osteoporosis is one of the possible long-term complications[4]. Sarcopenia, or loss of muscle mass and function, is a major cause of disability in diabetes[5]. Therefore, it is imperative to identify early sarcopenia, osteoporosis and their risk factors in older individuals with T2DM. Subsequently, suitable measures should be taken to avert and manage this ailment.

As a multifactorial systemic disease, many factors contribute to sarcopenia, such as age, sex, body mass index (BMI), duration of diabetes, glycemic control, nutritional status, and lifestyle[6-8]. Sarcopenia is commonly believed to be a decline in skeletal muscle mass and reduced muscle function that occurs with age. In sarcopenia research, the Asia Working Group for Sarcopenia (AWGS) suggests the utilization of the skeletal muscle index (SMI). This index is calculated by dividing the appendicular skeletal

muscle mass (ASMM) by the square of height, providing an adjusted measurement of muscle mass[9]. The factors associated with osteoporosis in T2DM include age, sex, BMI, serum vitamin D concentrations, lifestyle factors, duration of diabetes[10], and nutritional risk[11]. Since there are several common factors in osteoporosis and sarcopenia, many studies of the association between osteoporosis and skeletal muscle mass have been reported. The connection between low muscle mass and osteoporosis in patients with T2DM remains uncertain.

Malnutrition is frequently found in elderly individuals. Older adults with T2DM may face an increased risk of undernutrition due to excessively strict dietary habits aimed at managing blood sugar levels[12]. Various tools have been developed to assess malnutrition status, including the Malnutrition Screening Tool[13], Malnutrition Universal Screening Tool[14], Mini Nutritional Assessment Short Form[15], Nutrition Risk Score 2002[16], and Geriatric Nutritional Risk Index (GNRI)[17]. The GNRI has been utilized as a convenient and accessible method among these instruments for assessing outcomes, relying on serum albumin levels and the ratio of real body weight to ideal body weight.

The relationship between nutritional status and bone mass has been observed in different populations, such as individuals with chronic obstructive pulmonary disease[18], rheumatoid arthritis[19, 20], and ESRD[21]. In people with T2DM, nutrition, sarcopenia, and osteoporosis are rarely explored. Therefore, in this study, we investigated associations between BMD, the GNRI and body composition in patients with T2DM.

MATERIALS AND METHODS

Study design and participants

We conducted a retrospective cross-sectional study among T2DM patients admitted to the Department of Endocrinology, The Second Affiliated Hospital of Nantong University, between January 1, 2020, and March 1, 2022.

Patients

The main inclusion criterion in this study was T2DM. T2DM was defined as a fasting blood glucose (FBG) level of >7.0 mmol/L and/or a 2-h postprandial blood glucose level >11.1 mmol/L in an oral glucose tolerance test, in accordance with the 1999 World Health Organization (WHO) T2D diagnosis and classification criteria. the Patients were excluded based on the following criteria: (1) malignant tumor and severe heart, cerebral, liver or kidney diseases; (2) pituitary, thyroid, parathyroid and adrenal diseases; (3) treatment with glucocorticoids or sex hormones in the past 6 months; (4) concomitantly taking drugs affecting bone metabolism, such as calcium, vitamin D and bisphosphonates; and (5) unavailability of complete data on relevant variables and assessments. This study was approved by the ethics committee of The Second Affiliated Hospital of Nantong University and was in line with the Helsinki Declaration. The number for ethics approval was 2021KT063.

Data collection

Collection of demographic, medical, and laboratory data

All demographic information and relevant medical histories of the participants were recorded from their medical records. Demographic data included age, sex, height, weight and body mass index (BMI). Body weight and height were measured with the patient lightly clothed and without shoes. Body mass index (BMI; kg/m^2) was calculated as body weight in kilograms divided by height in meters squared. Medical history included diabetes duration, history of hypertension, and smoking and drinking history. The duration of diabetes was calculated by months from the time that the patient was diagnosed with T2DM in their medical records to the date we took blood tests. We also collected the glucose-lowering therapy status among participants. Glucose-lowering therapies were categorized as lifestyle alone and drug therapy. Hypoglycemic agents included insulin, insulin secretagogues, insulin sensitizers, metformin, α-glucosidase inhibitors (AGIs), dipeptidyl peptidase-4 inhibitors (DPP-4Is), sodium-glucose cotransporter-2 inhibitors (SGLT-2Is) and glucagon-like peptide-1 receptor agonists (GLP-1RAs).

For laboratory data collection, the nurses in the ward took blood samples from the antecubital vein in the early morning hours after overnight fasting (at least 8 h). Triglycerides (TGs, colorimetric method), total cholesterol (TC, cholesterol oxidase method), low-density lipoprotein cholesterol (LDL-C, selective melting method) and high-density lipoprotein cholesterol (HDL-C, enzyme modification method) were measured by an automatic biochemical instrument (Model 7600, Hitachi). The level of HbA1c was assessed by ion exchange high-performance liquid chromatography. The levels of bone metabolism markers, including osteocalcin (OS), β-collagen special sequence (β-CTX) and total type I procollagen N-terminal extension peptide (TP1NP). Additionally, other biochemical markers, such as serum creatinine (Cr), uric acid (UA), albumin and total bilirubin (TBil), were measured according to standard methodology.

BMD and body composition measurements

BMD and body composition were measured using dual energy X-ray absorptiometry (DXA) (Hologic-Discovery Wi, S/N86856). All of the patients were scanned, and calculations were performed by professionals in the corresponding medical and technical departments. According to the instrument manual, all operations were carried out in the standard mode: the patient lay flat and was scanned from head to feet. The measured indices included lumbar spine (L1-L4) BMD (LS-BMD), femoral neck BMD (FN-BMD), hip BMD (H-BMD), total (whole-body) bone mineral density (T-BMD), total body fat, the android/gynoid ratio, fat mass index, lean mass index and appendicular skeletal muscle index (ASMI). BMD (g/cm^2) was calculated using the following formula: bone mineral content (g)/area (cm^2); ASMI was calculated by limb skeletal muscle mass: appendicular skeletal muscle mass (kg)/height^2 (m^2); lean mass index was calculated using the following formula: lean mass (kg)/height^2 (m^2); and fat mass index was calculated using the following formula: fat mass (kg)/height^2 (m^2).

Calculation of the GNRI

Based on the serum albumin level and baseline body weight, the GNRI is calculated as follows: [redacted]. Ideal weight can be further calculated by the following equations:

Men: [redacted];

Women: [redacted].

Statistical analysis

The patients were classified by GNRI tertiles with cutoff values of < 101.85, 101.85 to 109.52, and > 109.52. A descriptive analysis of the data was performed based on the type of data, including the mean and standard deviation, and frequency and percentage. The trends of continuous data and categorical data were detected using one-way analysis of variance (ANOVA) with linear polynomial contrasts, Kruskal-Wallis tests, and Chi-squared tests with linear-by-linear associations. Furthermore, we generated scatter plots using GraphPad Prism to show the correlation between the Geriatric Nutritional Risk Index (GNRI) and bone mineral density (BMD), ASMI, and T-FAT. The factors associated with BMD and ASMI were identified using multiple stepwise linear regression analyses .

For the statistical analysis, we employed IBM SPSS Statistics (25.0) and GraphPad Prism (9.0).Statistical significance was determined using a *p*-value less than 0.05.

RESULTS

In this study, we enrolled 689 patients (57.2% men and 42.8% women), with a mean age of 55.59±10.88 years.

Patient characteristics

Table 1 shows comparisons of the characteristics of the patients classified by GNRI tertiles. Compared with patients in tertile 1, those in tertile 3 tended to be younger, had lower HbA1c and β-CTX, and had higher BMI, BMD, total body fat, android/gynoid ratio, fat mass index, lean mass index, ASMI, albumin, UA, TG, TC and TBil. These important trends persisted even when the patients were divided into younger and older subgroups (Tables 2-4).

Associations between GNRI, BMD, T-FAT and ASMI

Figure 1 shows the correlation between GNRI, BMD, T-FAT and ASMI in type 2 diabetes mellitus patients; the average BMD at the lumbar spine, femur neck and total

hip in men was higher than that in women (1.00 vs. 0.92, 0.81 vs. 0.73, 0.94 vs. 0.86, respectively, and all P<0.001); the GNRI was found to be positively and significantly associated with ASMI, T-FAT and BMD at all bone sites in men and women; Table 5 shows multiple linear regression models displaying associations of the GNRI with BMD; the fully adjusted Model 3 further adjusted for HbA1c, OS, β-CTX, TP1NP, albumin, Cr, UA, TG, TC, HDL-C, LDL-C, TBil, and the GNRI was significantly and positively associated with LS-BMD (b=0.040, t=2.492, P = 0.013, R^2=0.197) and FN-BMD (b=0.027, t=2.345, P = 0.019, R^2=0.341)

Figure 1.Scatter diagrams showing the correlation between GNRI, BMD, T-FAT and ASMI、

Multivariate forward linear regression analysis of the determinants of BMD and ASMI

Table 6 shows the determinants of BMD using multivariate stepwise linear regression analysis after adjusting for age, sex, height, weight, diabetes duration, hypertension, SBP, DBP, GNRI, BMI, HbA1c, OS, β-CTX, TP1NP, albumin, Cr, UA, TG, TC, HDL-C, LDL-C, TBil, ASMI, total body fat, android/gynoid ratio, fat mass index and lean mass index; the lean mass index was positively correlated with BMD at all bone sites; age, diabetes duration and β-CTX were negatively correlated with BMD at all bone sites; height and Cr were positively correlated with lumbar spine BMD, whereas albumin and ASMI were negatively correlated with lumbar spine BMD; albumin and the android/gynoid ratio were negatively correlated with femoral neck BMD, whereas height was positively correlated with femoral neck BMD; weight was positively correlated with total hip BMD, whereas the android/gynoid ratio was negatively correlated with total hip BMD

Table 7 shows the determinants of ASMI using multivariate forward linear regression analysis after adjusting for age, sex, height, weight, diabetes duration, hypertension, SBP, DBP, GNRI, BMI, HbA1c, OS, β-CTX, TP1NP, albumin, Cr, UA, TG, TC, HDL-C, LDL-C and TBil; in men, age, diabetes duration and HbA1c were negatively correlated with ASMI, whereas weight and BMI were positively correlated with ASMI; in women,

weight and OS were positively correlated with ASMI, whereas age, height, TBil and β-CTX were negatively correlated with ASMI

DISCUSSION

This study investigated associations among GNRI, BMD, and ASMI in T2DM patients. In this research, we discovered that proper nutrition, as denoted by a high GNRI, was linked to a lower HbA1c, higher BMD at all bone sites, higher lean mass index and higher ASMI. Based on prior research, this study utilized the GNRI and found that the GNRI was positively related to ASMI and BMD at all bone sites in type 2 diabetes mellitus patients. Additionally, a low lean mass index and higher β-CTX were associated with low BMD at all bone sites. Age was negatively correlated with ASMI, whereas weight was positively correlated with ASMI.

Despite the appropriate consumption, the nutrition of patients with type 2 diabetes mellitus was significantly impacted[22]. Diabetes speeds up the decline of muscle power, quality and serum albumin, highlighting the importance of maintaining a proper balance of protein and energy in one's diet. The current investigation demonstrated that a decreased GNRI posed a notable hazard for diminished BMD and ASMI among individuals with type 2 diabetes mellitus. This finding is consistent with previous studies[23]. Studies have demonstrated that the GNRI can be applied as a convenient and reliable indicator of the BMD and ASMI conditions of patients with chronic hepatitis C[24], postmenopausal women who have undergone total thyroidectomy[25] and patients receiving hemodialysis[26]. Therefore, the GNRI might be a convenient and reliable indicator of BMD and ASMI status in patients with type 2 diabetes mellitus. As albumin level reflects protein status and is a major component of the GNRI, the effect of protein on bone and muscle may help to explain the associations between GNRI, BMD and ASMI.

The second important finding of this study is that a low GNRI was associated with a higher HbA1c. This indicates that the presence of malnutrition is not conducive to blood sugar control. In addition to drug therapy, the basic treatment regimen for type 2 diabetes patients is diet restriction and exercise to achieve the goal of controlling blood sugar. Malnutrition can result if there is no strict and regular diet strategy. A previous study has proven that hyperglycemia contributes to the accelerated decline in muscle mass among patients with T2DM[27]. Higher HbA1c levels may lead to an increased risk of low muscle mass *via* a variety of mechanisms. The main causes include insulin resistance, inflammation, and the production of glycation end products. Therefore, nutritional balance is beneficial to control blood sugar and reduce the incidence of sarcopenia. Individuals with type 2 diabetes, especially the elderly, need individualized dietary strategies to reduce the incidence of malnutrition. Regular nutritional assessments are necessary. People with type 2 diabetes can avoid the adverse effects of malnutrition by adjusting their diet. [Editor1]

At all bone sites, there was a correlation between low BMD and a high level of β-CTX, which is the third significant discovery of this research. β-CTX is derived from the degradation of type I collagen, and its content in bone collagen is much higher than that in the rest of the tissue, so it can be more representative and more directly reflect the degradation of bone matrix collagen and be used as an indicator of bone resorption. Bone homeostasis depends on the resorption and formation of bones. Long-term hyperglycemia can affect the adhesion of osteoblasts to collagen, causing dysfunction of osteoblasts, inhibiting bone formation and accelerating bone resorption, causing an increase in PINP and β-CTX. This may explain our finding of an association between a high β-CTX level and low BMD. β-CTX plays a critical role in bone turnover and is a sensitive marker for the early diagnosis of OP.

Another important finding of this study is that age was negatively correlated with ASMI. Sarcopenia is the age- related loss of muscle mass, strength, and function[28]. Degenerative changes in the structure and function of the human neuromuscular system occur with age, and the presence of diabetes accelerates the decline in muscle

mass and strength through changes such as high levels of reactive oxygen species produced by oxidative stress and dysfunctional mitochondria. In this study, we also found a significant association between weight and ASMI. The majority of studies have shown that low BMI is also associated with sarcopenia[29]. Malnutrition, a potent risk factor for sarcopenia, could potentially account for the higher occurrence and frequency of sarcopenia in individuals with reduced body weight. Malnutrition, a potent risk factor for sarcopenia, might well explain the increased prevalence and incidence of sarcopenia in individuals with lower weight.

This study had multiple limitations. Because the study had a cross-sectional design, it was not possible to establish causal relationships. Furthermore, the participants chosen for this research encompassed both males and females spanning a wide age bracket of 21 to 81 years. T2DM patients of the same gender and age range have not been studied, but this study is closer to the clinical situation. In the end, we only included participants who were hospitalized; we did not evaluate muscle strength and quality.

CONCLUSION

Poor nutrition, as indicated by a low GNRI, was associated with low levels of AMSI and BMD at all bone sites in type 2 diabetes mellitus patients. Using the GNRI to evaluate nutritional status and using DXA to investigate body composition in patients with T2DM is of value in assessing bone health and physical performance.

ARTICLE HIGHLIGHTS

Research background

In people with T2DM, the association between nutrition, sarcopenia, and osteoporosis has rarely been explored.

Research motivation

The relationship between nutritional status and bone mass has been observed in different populations, including individuals with chronic obstructive pulmonary disease, rheumatoid arthritis, and end-stage renal disease (ESRD).

Research objectives

Assess the associations among nutrition, bone mineral density (BMD) and body composition in patients with T2DM

Research methods

A total of 689 patients with T2DM were included to perform a retrospective analysis. The general information and biochemical indices of these patients were statistically analyzed.

Research results

Those who had a high GNRI tended to be younger and had lower HbA1c, higher BMD at all bone sites, and higher ASMI.

Research conclusions

Poor nutrition, as indicated by a low GNRI, was associated with low levels of AMSI and BMD at all bone sites in type 2 diabetes mellitus patients.

Research perspectives

We used a retrospective study to explore the association between nutrition, sarcopenia, and osteoporosis in patients with T2DM.

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