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ORIGINAL ARTICLE

Retrospective Study

Sarcopenia-associated factors and their bone mineral density levels in middle-aged and elderly male type 2 diabetes patients

De-Qing Chen, Yong-Xin Wu, Ying-Xiao Zhang, Hai-Ling Yang, Huan-Huan Huang, Jiang-Yan Lv, Qian Xiao

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De-Qing Chen, Yong-Xin Wu, Ying-Xiao Zhang, Hai-Ling Yang, Qian Xiao, Department of Geriatrics, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400042, China

Huan-Huan Huang, Department of Nursing, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400042, China

Jiang-Yan Lv, Department of Endocrinology, The People's Hospital of Rongchang District, Chongqing 402460, China

Corresponding author: Qian Xiao, MD, Chief Doctor, Department of Geriatrics, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuanjiagang, Yuzhong District, Chongqing 400042, China. xiaoqian1956@126.com

Abstract

BACKGROUND

Chronic hyperglycemia can damage the microcirculation, which impairs the function of various organs and tissues and predisposes individuals to chronic complications. Sarcopenia (SP) is the age-related decline in muscle mass and function that contributes to the sequelae of type 2 diabetes. In particular, diabetic patients are at higher risk of SP because of insulin resistance, chronic inflammation, and decreased physical activity.

AIM

To identify SP-associated factors in middle-aged and elderly male type 2 diabetes mellitus (T2DM) patients and their correlation with bone mineral density (BMD).

METHODS

A retrospective analysis was conducted on 196 middle-aged and elderly male T2DM inpatients in the First Affiliated Hospital of Chongqing Medical University between June 2021 and June 2023, with 60 concurrent healthy individuals as the control group. Differences in general information, blood biochemistry, glycosylated hemoglobin, muscle strength, and detection rate of SP were compared between groups. The BMD, appendicular skeletal muscle (ASM), and fat mass, as well as grip strength and gait speed, were determined for each patient, and the ASM index (ASMI) was counted. The quantitative data were subjected to correlation and logistic regression analyses to identify risk factors for SP.

RESULTS
Fifty-one of the 196 middle-aged and elderly male T2DM patients were diagnosed with SP, which accounted for 26.02%. The middle-aged and elderly T2DM patients with SP exhibited a longer diabetes mellitus (DM) course and a lower body mass index (BMI) and 25(OH)D_3 compared with the non-SP patients. The T2DM + SP patients exhibited lower BMI, ASM, ASMI, left- and right-hand grip strength, gait speed, and muscle and fat mass of the upper and lower limbs compared with the diabetic non-SP patients. The femoral neck, total hip, and lumbar spine L_{1-4} BMD were markedly lower in T2DM + SP patients compared with those in the non-SP diabetics. Long-term DM course, low BMI, and low BMD of the femoral neck, lumbar spine L_{1-4}, and total hip were identified as risk factors for the development of SP.

CONCLUSION
T2DM patients are at risk for SP; however, measures can be taken to prevent the related risk factors.

Key Words: Male; Type 2 diabetes mellitus; Sarcopenia; Bone mineral density; Appendicular skeletal muscle

Core Tip: Type 2 diabetes mellitus (T2DM) and osteoporosis are common maladies in middle-aged and older adults. Individuals with T2DM are at a significantly higher risk of developing osteoporosis and falling and fracturing compared with healthy individuals. Sarcopenia is one of the most important factors for bone loss. A few studies have focused on the association between sarcopenia and osteoporosis in men with type 2 diabetes. Therefore, this study examined the association between sarcopenia and bone mineral density in middle-aged and elderly men with T2DM.

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INTRODUCTION

As a chronic condition characterized by hyperglycemia, diabetes mellitus (DM) is caused by impaired insulin secretion or functional defects[1]. Chronic hyperglycemia can damage the microcirculation, which disrupts the function of various organs and tissues and predisposes individuals to chronic complications[2]. The International Diabetes Federation reported that the global prevalence of DM in adults was 536.6 million in 2021, which may increase to 783.2 million by 2045[3]. Sarcopenia (SP), which occurs in older adults, is a disorder hallmarked by the progressive loss of skeletal muscle mass and function[4,5]. After the third decade of life, muscle mass decreases by 1% per year[6]. SP occurs when the loss becomes excessive and accelerates, leading to the deterioration and impairment of muscle function[7]. The loss of skeletal muscle mass and function severely compromises an individual's physical health and quality of life. This results in difficulties in daily activities, increases the risk of falls and fractures and reduces life expectancy in older adults[8]. SP and type 2 DM (T2DM) are more prevalent with age and predispose patients to long-term complications, frailty, hospitalization, and premature death[9]. SP is the age-related decline in muscle mass and function, which contributes to the cause and consequences of type 2 diabetes[10]. In particular, diabetic patients are at higher risk for SP because of insulin resistance, chronic inflammation, and decreased physical activity. Moreover, SP disrupts glycemic control and exacerbates the development of DM, resulting in various complications[11].

Middle-aged and elderly T2DM patients are at a 2- to 3-fold higher risk of developing SP compared with healthy individuals. This is associated with altered muscle mass and function because of insulin resistance, chronic inflammation, and oxidative stress[12]. SP is considered a new complication observed in elderly patients with T2DM[9]. T2DM with osteoporosis in middle-aged and elderly patients causes long-term physical pain and functional decline, which increases the risk of fractures and disability. In a study of 1090 Chinese residents over the age of 60 years, T2DM was significantly associated with an increased likelihood of developing SP and pre-sarcopenic conditions. It is also associated with glycemic control levels, duration of DM, physical activity, hypoglycemic drugs, and DM-related chronic complications [13]. Pechmann *et al*[14] found that patients with T2DM who exhibit proteinuria, osteoporosis, and increased adiposity are more susceptible to SP. This highlights the need to evaluate SP in patients with T2DM to implement early measures for the prevention or treatment of this condition; however, studies on the risk factors for the development of SP in middle-aged and older men with type 2 diabetes are incomplete. Moreover, studies have shown that the prevalence of SP is slightly higher in men compared with women in the Chinese population[13]. In addition, postmenopausal osteoporosis is present in women, with greater levels of hormonal influence compared with men[15]. Therefore, to better understand SP in combination with T2DM for the middle-aged and elderly male population and achieve effective early screening and intervention, we identified factors associated with SP in these patients and their correlation with bone mineral density (BMD).

MATERIALS AND METHODS

Research participants

A retrospective analysis was conducted on 196 middle-aged and elderly male T2DM inpatients in the First Affiliated Hospital of Chongqing Medical University between June 2021 and June 2023. The inclusion criteria were as follows: (1) All patients were male; (2) Aged 60-80 years; (3) Basic self-care ability, normal cognitive function, and barrier-free communication; (4) BMD measured by dual-energy X-ray absorptiometry (DXA); and (5) Complete medical records. The exclusion criteria were as follows: (1) Type 1 DM; (2) Severe DM-associated complications; (3) Other systemic diseases or tumors; (4) Inability to carry out the grip strength (GS) or six-minute walk test (6MWT); (5) Orthopedic disorders (*e.g.*, lumbar disk herniation and fracture) that seriously affect limb movements; (6) Diseases affecting bone or calcium metabolism or recent use of drugs that affect bone metabolism; and (7) Defective clinical data, were excluded. In addition, 60 non-diabetic middle-aged and older men who concurrently underwent check-ups were selected as the control group.

Patient data collection

Baseline data: General clinical baseline data including age, sex, body mass index (BMI), and DM course of the subjects were collected. After heparin anticoagulation of the fasting venous blood samples collected from the subjects, biochemical indices, including fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), and high/Low-density lipoprotein (HDL/LDL), were measured using an automatic biochemical analyzer (Hitachi 7600, Hitachi). Glycosylated hemoglobin (HbA1c) was quantitated by high-pressure liquid chromatography and 25(OH)D_3 was measured by an enzyme-linked immunoassay.

DXA: The muscle and fat content as well as the BMD of various body parts were measured by DXA (Lunar iDXA, GE, United States). Appendicular skeletal muscle mass (ASM) is the sum of the upper and lower limb skeletal muscle contents. The ASM index (ASMI) is defined as ASM (kg)/height^2 (height, m), namely ASM/H^2. Referring to the European Working Group on SP in Older People (EWGSOP2) diagnostic criteria[16] and the results of other studies, such as that by Verschureren[17], the cut-off value for a diagnosis of SP in men is considered ASMI ≤ 7.26 kg/m^2, whereas the requirements for low GS or gait speed. Severe patients meet all of the above three conditions.

Measurement and evaluation of GS: The muscle strength of the subjects was evaluated by the GS test with a Jamar dynamometer, and the measurement unit was in kg. During the measurement, the patient sat upright, with their feet naturally placed on the ground, the knees, hips, and elbows bent by 90°, the upper arms flat with the chest, the forearms neutral, and the wrists extended by 0°-30°. The GS test was repeated three times for each hand, with the maximum value used for the analysis. The definition of a low GS in patients with different BMIs was ≤ 29 kg for patients with a BMI ≤ 24 kg/m^2, ≤ 30 kg for those with a BMI > 24 kg/m^2 but ≤ 28 kg/m^2, and ≤ 32 kg for those with a BMI > 28 kg/m^2.

Physical function evaluation: This evaluation was conducted using the 6MWT. A marker was used to draw a 12 m straight line on the flat ground and marked the starting point, the 3 and 9 m points, and the terminal point. The timing began as the starting point and the subject walked to the 3 m line and ended when the subject walked to the 9 m line. Three tests were conducted and the fastest gait speed was included in the statistics, with < 0.8 m/second considered a low pace.

Grouping information

Based on the diagnostic criteria of the EWGSOP and the results of studies, such as those of Verschureren, the cut-off value for the diagnosis of SP in men is considered ASMI ≤ 7.26 kg/m^2, while meeting the requirements of low GS or gait speed. For severe patients, the above three conditions were met. T2DM cases were assigned to SP and non-SP groups for a follow-up study.

Statistical analysis

The data were imported into SPSS 25.0 for data analysis. The quantitative data (represented by the mean ± SD) were tested by independent sample *t*-tests, and count data (described as rates) were tested by a χ^2 test. The correlation of BMD with other factors was determined by Spearman correlation and multivariate logistic regression analyses. Taking $\alpha = 0.05$ as the significance level, $P < 0.05$ indicated the presence of statistically significant differences.

RESULTS

General data of T2DM patients and controls

As listed in Table 1, T2DM patients were not markedly different from healthy controls in age, TC, TG, and BMD of the femoral neck and lumbar spine L_{1-4} ($P > 0.05$); However, T2DM patients exhibited lower HDL, LDL, 25(OH)D_3, and total hip BMD compared with the controls as well as higher FBG and HbA1c ($P < 0.05$).

General data of T2DM patients complicated by SP

SP was diagnosed in 51 (26.02%) of the 196 middle-aged and elderly male T2DM patients. The DM course was longer in the T2DM + SP patients compared with the non-SP counterparts, and BMI and 25(OH)D_3 were lower ($P < 0.05$); however, the two groups showed no significant inter-group differences in age, FBG, HbAlc, and other biochemical indexes ($P >$

Table 1 General characteristics between type 2 diabetes mellitus patients and controls

	T2DM (*n* = 196)	Control (*n* = 60)	*t*	*P* value
Age (years)	72.06 ± 4.87	71.82 ± 4.28	0.349	0.723
Course of diabetes mellitus (years)	15.24 ± 2.08	-		
BMI (kg/m^2)	24.58 ± 2.47	25.04 ± 2.45	1.261	0.208
FBG (mmol/L)	9.69 ± 2.30	5.34 ± 0.60	14.49	< 0.0001
HbA1c (%)	9.14 ± 1.78	5.64 ± 0.85	14.74	< 0.0001
Total cholesterol (mmol/L)	4.27 ± 1.39	4.64 ± 1.03	1.897	0.059
Triglyceride (mmol/L)	1.73 ± 0.81	1.84 ± 0.61	0.967	0.335
High-density lipoprotein (mmol/L)	1.13 ± 0.30	1.26 ± 0.26	2.907	0.004
Low-density lipoprotein (mmol/L)	2.51 ± 0.92	2.86 ± 0.67	2.662	0.008
25(OH)D_3 (ng/mL)	21.87 ± 7.85	31.42 ± 9.33	7.875	< 0.0001
Femoral neck BMD	0.76 ± 0.13	0.79 ± 0.12	1.469	0.143
Total hip BMD	0.87 ± 0.14	0.95 ± 0.11	3.855	0.0001
Lumbar spine L_{1-4} BMD	0.91 ± 0.20	0.97 ± 0.16	1.612	0.108

T2DM: Type 2 diabetes mellitus; BMD: Bone mineral density; BMI: Body mass index; FBG: Fasting blood glucose; HbA1c: Glycosylated hemoglobin.

0.05; Table 2).

Body composition and functional indices of diabetic patients with SP

The BMI, ASM, ASMI, left- and right-hand GS, gait speed, upper and lower limb muscle mass, and upper and lower limb fat mass were significantly lower in diabetic patients with SP compared with those without SP ($P < 0.05$; Table 3).

BMD in diabetic patients with SP

T2DM + SP patients exhibited a statistically lower femoral neck, total hip, and lumbar spine L_{1-4} BMD value than the T2DM cases without SP ($P < 0.05$; Figure 1).

Correlation between BMD of different body parts and body function in diabetic patients

The femoral neck and lumbar spine L_{1-4} BMD of middle-aged and elderly male T2DM patients were positively correlated with muscle mass, GS, gait speed, and fat mass; however, no significant correlation was identified between total hip BMD and lower limb fat mass (Table 4).

Influencing factors for SP in diabetic patients

A multivariate regression analysis was performed on the variables with significant differences in Table 2 and Table 4, with SP (0 = non-SP; 1 = SP) as the dependent variable and DM course, BMI, 25(OH)D_3, and BMD as independent variables. Continuous variables were converted into categorical variables based on each median value for logistic regression. The results indicated that long-term DM course and low BMI, as well as low femoral neck, lumbar spine L_{1-4}, and total hip BMD were risk factors for SP (Table 5).

DISCUSSION

Senile SP and DM are intricately linked and negatively affect one another[18]. Feng *et al*[19] found that the overall prevalence of SP was as high as 18% in diabetic patients, which is a condition that requires early intervention. This study aimed to identify the influencing factors of SP in T2DM, which will assist clinicians and nutritionists to identify and intervene early, and ultimately improve overall patient health and well-being.

SP was diagnosed in 51 (26.02%) of the 196 middle-aged and elderly men with T2DM, similar to the SP prevalence of 19% in male T2DM patients over 60 years reported by Kim *et al*[20]. In addition, middle-aged and elderly T2DM patients with SP have a significantly longer DM course compared with those without SP as well as a statistically lower BMI and 25(OH)D_3. BMI, ASM, ASMI, left- and right-hand GS, gait speed, upper- and lower limb muscle, and fat mass were significantly lower in DM patients with SP compared with non-SP patients. In addition, significantly reduced femoral neck, total hip, and lumbar spine L_{1-4} BMD content were assessed in diabetic patients with SP compared with those without SP. Skeletal muscle accounts for over 40% of the human body weight and plays an important role in glucose metabolism. Normal glucose metabolism is also necessary for maintaining the normal structure and physiological

Table 2 Comparison between type 2 diabetes mellitus patients with and without sarcopenia

	Sarcopenia group (*n* = 51)	Non-sarcopenia group (*n* = 145)	*t*	*P* value
Age (years)	71.41 ± 4.87	72.29 ± 4.87	1.108	0.269
Course of diabetes mellitus (years)	16.84 ± 3.31	14.68 ± 0.91	7.130	< 0.0001
BMI (kg/m^2)	23.11 ± 2.1	25.10 ± 2.36	5.263	< 0.0001
FBG (mmol/L)	9.59 ± 2.31	9.72 ± 2.30	0.369	0.712
HbA1c (%)	9.14 ± 1.71	9.15 ± 1.81	0.010	0.992
Total cholesterol (mmol/L)	3.99 ± 1.24	4.37 ± 1.43	1.668	0.097
Triglyceride (mmol/L)	1.54 ± 0.73	1.80 ± 0.83	1.239	0.217
High-density lipoprotein (mmol/L)	1.09 ± 0.25	1.15 ± 0.32	1.153	0.250
Low-density lipoprotein (mmol/L)	2.42 ± 0.86	2.55 ± 0.94	0.884	0.378
25(OH)D_3 (ng/mL)	19.17 ± 6.39	22.82 ± 8.11	2.917	0.004

BMI: Body mass index; FBG: Fasting blood glucose; HbA1c: Glycosylated hemoglobin.

Table 3 Comparison of body composition and functional indexes

	Sarcopenia group (*n* = 51)	Non-sarcopenia group (*n* = 145)	*t*	*P* value
BMI (kg/m^2)	23.11 ± 2.1	25.10 ± 2.36	5.263	< 0.0001
ASM (kg)	19.10 ± 1.60	23.42 ± 2.73	10.66	< 0.0001
ASMI (kg/m^2)	6.50 ± 0.48	8.28 ± 0.52	21.44	< 0.0001
Left-hand grip strength (kg)	25.45 ± 4.03	37.68 ± 4.82	16.23	< 0.0001
Right-hand grip strength (kg)	26.45 ± 2.72	39.02 ± 4.76	17.86	< 0.0001
Gait speed (m/s)	0.60 ± 0.16	1.27 ± 0.16	25.91	< 0.0001
Upper limb muscle mass (kg)	4.82 ± 0.45	5.93 ± 0.75	10.02	< 0.0001
Lower limb muscle mass (kg)	15.13 ± 1.28	17.74 ± 1.57	10.68	< 0.0001
Upper limb fat mass (kg)	2.58 ± 0.49	3.00 ± 0.47	5.398	< 0.0001
Lower limb fat mass (kg)	4.57 ± 1.25	5.59 ± 1.49	4.398	< 0.0001

BMI: Body mass index; ASM: Appendicular skeletal muscle; ASMI: Appendicular skeletal muscle index.

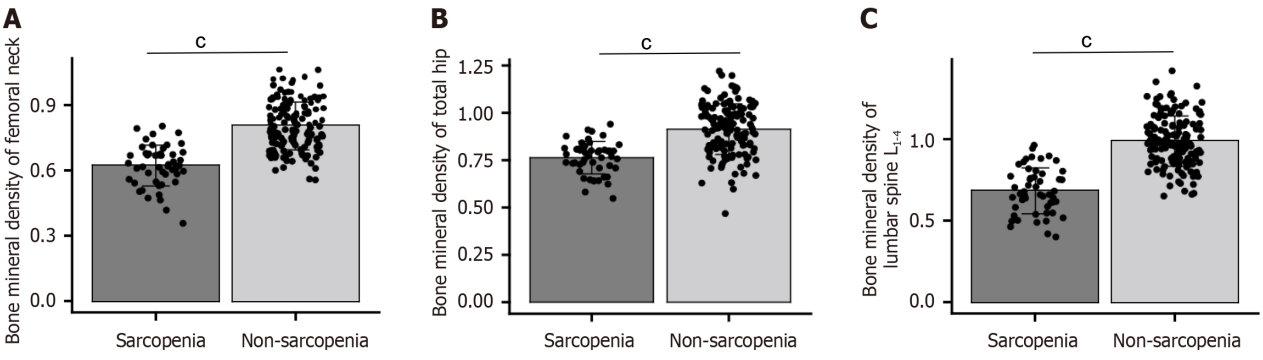

Figure 1 Comparison of bone mineral density. A: Bone mineral density of femoral neck; B: Bone mineral density of total hip; C: Bone mineral density of lumbar spine L_{1-4}. $^cP < 0.001$.

Table 4 Correlation between bone mineral density and function in different body parts of diabetic patients

	Femoral neck		Total hip		Lumbar spine L_{1-4}	
	r	*P* value	*r*	*P* value	*r*	*P* value
ASM (kg)	0.348	< 0.0001	0.309	< 0.0001	0.422	< 0.0001
ASMI (kg/m^2)	0.557	< 0.0001	0.407	< 0.0001	0.582	< 0.0001
Left-hand grip strength (kg)	0.487	< 0.0001	0.398	< 0.0001	0.557	< 0.0001
Right-hand grip strength (kg)	0.453	< 0.0001	0.455	< 0.0001	0.598	< 0.0001
Gait speed (m/s)	0.538	< 0.0001	0.455	< 0.0001	0.612	< 0.0001
Upper limb muscle mass (kg)	0.438	< 0.0001	0.246	0.0005	0.368	< 0.0001
Lower limb muscle mass (kg)	0.447	< 0.0001	0.356	< 0.0001	0.449	< 0.0001
Upper limb fat mass (kg)	0.264	0.0002	0.155	0.030	0.233	0.001
Lower limb fat mass (kg)	0.196	0.006	0.114	0.111	0.296	< 0.0001

ASM: Appendicular skeletal muscle; ASMI: Appendicular skeletal muscle index.

Table 5 Logistic regression analysis of sarcopenia in diabetic patients

Factors	β	SE	Wald	*P* value	HR	95%CI
DM course (> 14.8)	1.719	0.594	8.386	0.004	5.580	1.743-17.866
BMI (≤ 24.8)	1.275	0.602	4.480	0.034	3.577	1.099-11.644
25(OH)D_3 (≤ 21.58)	0.362	0.580	0.389	0.533	1.436	0.461-4.475
Femoral neck BMD (≤ 0.76)	2.610	0.703	13.776	0.000	13.594	3.427-53.929
Total hip BMD (≤ 0.86)	2.457	0.662	13.785	0.000	11.668	3.190-42.682
Lumbar spine L_{1-4} BMD (≤ 0.92)	4.049	0.876	21.383	0.000	57.331	10.306-318.929
Constant	-9.480	1.470	40.613	0.000	0.000	-

DM: Diabetes mellitus; BMI: Body mass index; HR: Hazard ratio; BMD: Bone mineral density.

function of the skeletal muscle[21]. Decreased skeletal muscle mass results in a decrease in the amount of GLUT-4 in skeletal muscle cell membranes, which reduces glucose uptake in the blood and sustains the elevation of blood glucose levels[22]. Vitamin D (VD) plays a role in bone and muscle homeostasis by modulating calcium-phosphorus metabolism and maintaining normal bone mineral content[23]. VD receptor expression on the skeletal muscle fiber cell membrane decreases with age and exacerbates VD deficiency in older adults, a condition associated with enhanced bone resorption, reduced muscle mass, and loss of strength[24]. Moreover, because of the synchronous physical-mechanosensory effects of muscle and bone mass, muscle mass is positively correlated with BMD. Thus, SP patients are three times more likely to suffer from osteoporosis compared with those exhibiting normal muscle mass[25]. In the present, the femoral neck and lumbar spine L_{1-4} BMD were positively correlated with muscle mass, GS, gait speed, and fat mass, which is consistent with the theory that muscle and bone change simultaneously. Moreover, changes in muscles and bones can also be affected by growth hormones, cytokines, inflammatory responses, and other factors.

Using a multivariate analysis, we found that a long-term DM course, low BMI, and low BMD of the femoral neck, lumbar spine L_{1-4}, and total hip are risk factors for SP. The longer the DM course, the higher the incidence of DM-induced chronic complications, such as diabetic nephropathy, diabetic neuropathy, and diabetic osteoporosis, and the higher the SP risk. Despite the increasing prevalence of obesity and SP in older adults[26], it was reported that a larger muscle mass in overweight and obese elderly people does not impart functional advantages[27]. An inverse connection between BMI and SP has been reported[28,29], which suggests that the incidence of SP decreases concomitantly with increased BMI. Therefore, we conclude that BMI does not distinguish between fat mass, fat-free mass, and fat distribution[30]. Furthermore, body weight may offer protection against SP.

One limitation of this study is the sample size was small, thus further large-scale studies are needed to validate whether there is a high BMI-protective advantage in the prevalence of SP in the Chinese population. In another study, there was a negative association between lumbar BMD and SP in 8386 participants aged 20 to 59 years[31]. BMD decreases with age and is an important factor affecting human lipid mass, muscle mass, and bone mineral content.

CONCLUSION

In summary, patients with a long-term DM course, low BMI, and low BMD of the femoral neck, spine L_{1-4}, and total hip have an increased risk of developing SP. Older men with T2DM combined with SP are at increased risk of developing osteoporosis. These patients should be screened early for dietary and potential clinical interventions to reduce the risk of fracture, which provides a scientific basis for future studies. For T2DM patients, appropriate resistance training, increased protein intake, and blood glucose control should be carried out to delay the occurrence of diabetic complications and reduce the risk of SP.

FOOTNOTES

Author contributions: Chen DQ, Wu YX, Zhang YX and Yang HL contributed to the conception and design; Chen DQ, Huang HH, Lv JY and Xiao Q contributed to the analysis and interpretation of data; Chen DQ and Xiao Q contributed to the writing, review, and/or revision of the manuscript; All authors contributed to the acquisition of data (acquired and managed patients) and final approved the manuscript.

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ORCID number: De-Qing Chen 0009-0003-4019-0224; Yong-Xin Wu 0000-0003-0146-1389; Ying-Xiao Zhang 0000-0003-2511-7638; Qian Xiao 0009-0007-8981-2767.

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