

A cross-sectional study: an assessment of low muscle mass and osteoporosis in type 2 diabetes mellitus patients with a high glycated hemoglobin level

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Abstract

Background: Low muscle mass and osteoporosis are commonly observed in individuals with type 2 diabetes mellitus (T2DM). We investigated the prevalence of low muscle mass and osteoporosis in patients with T2DM who had high glycated hemoglobin (HbA1c) levels.

Methods: We included 187 Chinese patients with T2DM who were aged ≥ 50 years and evaluated their body composition using dual-energy X-ray absorptiometry. We measured levels of fasting blood glucose, HbA1c, B collagen-specific sequences (B-CTX), osteocalcin (OC), propeptide of type 1 procollagen (P1NP), and 25-hydroxy vitamin D.

Results: Of the total patients, 82 were men and 105 were women. The prevalence rates of low muscle mass, osteopenia, and osteoporosis were 35.8%, 38.0%, and 31.0%, respectively. The prevalence rate of low muscle mass was significantly higher in women with HbA1c levels $>9.0\%$ than in those with HbA1c levels $<9.0\%$. The prevalence rates of osteopenia and osteoporosis in men with HbA1c levels $>9.0\%$ differed significantly from those with HbA1c levels $<9.0\%$. The appendicular skeletal muscle mass index (ASMI), trunk muscle mass, lumbar spinal bone mineral content (BMC), lumbar spine BMD, femoral BMC, and femoral BMD were significantly decreased, and the serum levels of B-CTX, OC, and P1NP were significantly increased in patients with T2DM who had osteoporosis. The ASMI was associated with osteopenia/osteoporosis in men and women with T2DM.

Conclusions: In patients with T2DM, high HbA1c levels were associated with higher prevalence rates of low muscle mass in women and osteoporosis in men, and ASMI was a risk factor of osteoporosis.

Keywords: glycated hemoglobin, low muscle mass, osteoporosis, type 2 diabetes mellitus

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Introduction

China has nearly 20% of the global population, while the proportion of the elder population in China is 15.5%.¹ The prevalence rates of diabetes among individuals aged 40–59 and >60 years are 12.9% and 20.2%, respectively.² Type 2 diabetes mellitus (T2DM) is a chronic inflammatory disease characterized by glucose metabolism disorders and insulin resistance. Blood glucose disorders and their related complications affect the quality of life of elderly patients.

In patients with T2DM, skeletal muscle is significantly reduced.³ Patients with low muscle mass are at increased risk of falls and fractures, which can lead to incapacitation, dependence, and even death.⁴ Limb muscle mass in patients with diabetes is very low.³ In a previous study, the prevalence of low muscle mass in patients with T2DM was high.⁵ The prevalence rate of low muscle mass was 14.4% in a Chinese population with T2DM and significantly higher than in those without T2DM.⁶

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Osteoporosis is also a common disease correlated with aging; its incidence increases with age. T2DM and osteoporosis are affected by age and lifestyle and are more commonly observed in elderly individuals. The Rotterdam study investigated data on bone mineral density (BMD) and fracture in 792 patients with T2DM and 5863 nondiabetic patients. The results showed that patients with T2DM had higher femoral and lumbar spine BMD, but the risk of fracture was increased 1.33 times.⁷ In a previous study, the incidence rates of hip, vertebral, and forearm fractures in patients with T2DM and osteoporosis were significantly increased, compared with patients who had osteoporosis but not T2DM.⁸

Patients with low muscle mass are at increased risk of falls and fractures.⁹ The association between low muscle mass and osteoporosis in patients with T2DM, particularly those with poor blood glucose control, is unclear. Glycated hemoglobin (HbA1c) is an important indicator of diabetes management. HbA1c levels reflect the average glycemic value over approximately 3 months and has a direct relationship with diabetic complications. In this study, we investigated the association between low muscle mass and osteoporosis in patients with T2DM who had high HbA1c levels.

Materials and methods

Study design and participants

We conducted a retrospective cross-sectional study among patients admitted to the Department of Endocrinology, Kunshan Hospital Affiliated with Jiangsu University, between 1 December 2018 and 31 December 2020.

Patients

The inclusion criteria in this study were patients with T2DM and aged ≥ 50 years. 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 World Health Organization (WHO) 2006 criteria. The exclusion criteria were patients with thyroid disease, renal failure, and cerebral infarction, in addition to those who had received anti-osteoporosis therapies and hormone therapies such as growth

hormones, thyroid hormones, and sex hormones. This study was approved by the ethics committee of Kunshan Hospital Affiliated with Jiangsu University. The numbers for ethics approval was 2019-04-010-K01. All participants provided a written informed consent.

Parameters

Participants' weight, height, and systolic blood pressure were measured using standardized equipment. Information about the course of diabetes was collected from the medical records.

Dual-energy X-ray absorptiometry (DXA)

Whole-body dual-energy X-ray absorptiometry (DXA; Hologic Discovery, USA) was used to measure trunk muscle mass, body fat content, bone mineral content (BMC) and BMD of the lumbar spine and hip, appendicular skeletal muscle mass index (ASMI), and the ratio of skeletal muscle mass and body mass. ASMI was calculated using the following formula: appendicular skeletal muscle mass (ASM; kg)/height² (m²). The ratio of skeletal muscle mass and body mass was calculated using the following formula: skeletal muscle mass (kg)/body weight (kg). The diagnostic criterion for low muscle mass in Asian populations is an ASMI of <7.0 kg/m² in men and <5.4 kg/m² in women.¹⁰ The *T* scores were calculated with the database of DXA of Hologic discovery. Normal bone mass was defined as a *T* value > -1.0 ; osteopenia, as $-1.0 > T$ value > -2.5 ; and osteoporosis, as a *T* value of < -2.5 .

Laboratory examination

Fasting blood samples of participants were collected to determine the levels of FBG, HbA1c, serum creatinine, B collagen-specific sequences (B-CTX), osteocalcin (OC), propeptide of type I procollagen (P1NP), and 25-hydroxy vitamin D.

Statistical analyses

We used IBM SPSS Statistics version 22 for the statistical analysis (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean \pm standard deviation (SD). The variables that were not normally distributed are expressed as median (interquartile range [IQR]). For comparison of normal distribution variables between

the groups, the Student *t*-test was used. The Kruskal–Wallis test was used to compare if the data were not normally distributed. Categorical variables are expressed as percentages and were analyzed using a χ^2 test. Multivariable logistic regression analysis was performed to assess factors associated with osteopenia/osteoporosis; a step-by-step process was used to select covariates. Using a logistic regression model, the odds ratio (OR) and 95% confidence intervals (CIs) were calculated. A *p*-value of <0.05 was considered statistically significant.

Results

We enrolled a total of 212 inpatients with T2DM aged ≥ 50 years in the study. Eight participants were excluded because of severe diabetes complications (diabetic peripheral neuropathy, $n=7$; diabetic foot, $n=1$); 10 individuals refused to participate, five were excluded for incomplete data, and two were excluded for incorrect data. As a result, we analyzed data for 187 participants.

Among the participants, 82 were men and 105 were women, with a mean age of 64.58 ± 8.76 years. The mean duration of T2DM was 12.84 ± 7.83 years. The levels of HbA1c ranged from 4.7% to 15.6%, while the mean HbA1c level of all patients was $8.56 \pm 1.98\%$. Table 1 shows the clinical characteristics of the participants. Compared with men, women had lower height and weight and higher levels of serum BCTX, OC, and P1NP. Women had more body fat and a lower ASMI than men. In addition, the BMC and BMD of the lumbar spine and femur in women were significantly lower than those in men.

Among the participants, 67 (35.8%) were diagnosed as having low muscle mass, 71 (38.0%), as having osteopenia, and 58 (31.0%), as having osteoporosis. The prevalence rate of low muscle mass was significantly higher in women with HbA1c levels $>9.0\%$ than in those with HbA1c levels $<9.0\%$ (35.0% *versus* 16.9%, $p=0.035$). In addition, the prevalence rates of osteopenia and osteoporosis differed significantly between men with HbA1c levels $<9.0\%$ and those with HbA1c levels $>9.0\%$ (32.1% *versus* 62.1% and 17.0% *versus* 10.3%, respectively; $p=0.032$; Table 2).

According to the BMD *T* value measured on DXA, patients with T2DM were divided into normal BMD ($T > -1.0$), osteopenia ($-1.0 > T > -2.5$),

and osteoporosis ($T < -2.5$) groups. Height and weight were significantly reduced and serum BCTX and PINP levels significantly increased in the osteoporosis and osteopenia groups, as compared with the normal BMD group. ASMI, trunk muscle mass, lumbar spine BMC, lumbar spine BMD, femoral BMC, and femoral BMD were significantly decreased in the osteoporosis and osteopenia groups. Compared with the normal group, patients in the osteoporosis group had higher levels of serum OC (Table 3).

Multivariate logistic regression analysis was performed for osteopenia/osteoporosis in patients with T2DM. In the multivariate logistic analysis in men, ASMI and levels of P1NP were important risk factors for osteopenia/osteoporosis. In the multivariate logistic analysis in women, ASMI was a risk factor for osteopenia/osteoporosis (Table 4).

Discussion

In this study, we found that the prevalence of low muscle mass was 35.8%, the prevalence of osteopenia was 38%, and the prevalence of osteoporosis was 31.0%. The prevalence of osteopenia and osteoporosis in men with T2DM and HbA1c $>9.0\%$ was higher than that in men with T2DM and HbA1c $<9.0\%$. The prevalence of low muscle mass in women with T2DM and HbA1c $>9.0\%$ was higher than that in women with T2DM and HbA1c $<9.0\%$. Compared with T2DM patients who had normal BMD, ASMI and trunk muscle mass were significantly reduced in patients with T2DM and osteopenia and osteoporosis, while serum levels of B-CTX, OC, and P1NP were significantly increased in patients with T2DM and osteoporosis. Multivariate logistic regression analysis showed that ASMI was a risk factor for osteoporosis/osteopenia in men and women with T2DM.

Both T2DM and osteoporosis are metabolic diseases with a complex relationship. In this study, the prevalence of osteopenia and osteoporosis was 38% and 31.0%, respectively. A meta-analysis found that the prevalence of osteoporosis in patients with T2DM on the Chinese mainland was 44.8% in women and 37.0% in men,¹¹ which was higher than the prevalence of primary osteoporosis reported by Zeng *et al.*¹² In patients with T2DM, the change in BMD appears contradictory and there is no clear explanation. In different studies, BMD was increased, decreased, or

Table 1. Characteristics of T2DM patients stratified by gender.

	Men	Women	p-value
<i>n</i>	82	105	
Age (years)	65.23 ± 9.34	65.08 ± 8.28	0.372
Duration of diabetes (years)	13.00 (8.00, 19.00)	12.00 (6.00, 20.00)	0.693
Height (cm)	168.00 ± 6.12	155.57 ± 5.20	0.000
Weight (kg)	70.44 ± 10.85	63.02 ± 9.64	0.000
BMI (kg/m ²)	24.97 ± 3.99	25.61 ± 3.62	0.259
SBP (mmHg)	136.28 ± 20.378	142.03 ± 21.94	0.068
DBP (mmHg)	77.30 ± 15.492	78.05 ± 10.34	0.695
FBG (mmol/l)	7.64 (6.16, 9.67)	7.68 (5.98, 10.10)	0.642
HbA1c (%)	8.00 (6.70, 9.48)	8.6 (7.4, 9.5)	0.143
Serum creatinine (μmol/l)	66.59 ± 13.02	55.57 ± 14.86	0.000
BCTX (ng/ml)	0.22 (0.16, 0.31)	0.28 (0.21, 0.40)	0.000
OC (ng/ml)	9.00 (7.50, 11.50)	12.00 (9.00, 17.00)	0.000
P1NP (ng/ml)	30.00 (24.00, 38.50)	38.00 (29.00, 58.50)	0.000
25-OH-D (ng/ml)	22.62 ± 8.42	20.39 ± 7.67	0.064
Body fat (%)	27.20 ± 7.82	34.90 ± 5.24	0.000
ASMI (kg/m ²)	7.03 ± 0.97	5.98 ± 0.76	0.000
Trunk MM (kg)	24.16 ± 31.33	19.19 ± 24.67	0.077
S/B (%)	62.90 ± 5.05	54.72 ± 5.27	0.000
Lumbar spine BMC (g)	71.10 ± 14.02	50.00 ± 11.23	0.000
Femur BMC (g)	36.63 ± 6.45	25.78 ± 7.03	0.000
Lumbar spine BMD (g/cm ²)	1.01 ± 0.17	0.86 ± 0.15	0.000
Femur BMD (g/cm ²)	0.90 ± 0.12	0.80 ± 0.12	0.000

Data are expressed as the mean ± standard deviation or IQR.
 25-OH-D, 25-hydroxyvitamin D; ASMI, appendicular skeletal muscle index; B-CTX, B collagen specific sequences; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting plasma glucose; HbA1c, glycated hemoglobin; OC, osteocalcin; P1NP, propeptide of type 1 procollagen; S/B, the ratio of skeletal muscle mass and body mass; SBP, systolic blood pressure; Trunk MM, trunk muscle mass.

remained normal.^{13–15} The risk of fractures is higher in patients with T2DM than in patients without diabetes. The relative risks of hip fracture, vertebral fracture, and all fractures in patients with T2DM is increased by 1.27, 1.74,

and 1.22, respectively.¹⁶ A decrease in bone strength and microarchitecture may cause an increased risk of fracture in patients with T2DM. In a cross-sectional study, bone microstructure was measured using high-resolution peripheral

Table 2. The prevalence of pre-sarcopenia and osteoporosis in T2DM patients stratified by gender, age, HbA1c. *n* (%).

	HbA _{1c}	Normal	Low muscle mass	<i>p</i> -value	Normal	Osteopenia	Osteoporosis	<i>p</i> -value
Men	<9.0% (<i>n</i> =53)	27 (50.9)	26 (49.1)	0.596	27 (50.9)	17 (32.1)	9 (17.0)	0.032
	≥9.0% (<i>n</i> =29)	13 (44.8)	16 (55.2)		8 (27.6)	18 (62.1)	3 (10.3)	
	Total (<i>n</i> =82)	40 (48.8)	42 (51.2)		35 (42.7)	35 (42.7)	12 (14.6)	
Women	<9.0% (<i>n</i> =65)	54 (83.1)	11 (16.9)	0.035	18 (27.7)	23 (35.4)	24 (36.9)	0.105
	≥9.0% (<i>n</i> =40)	26 (65.0)	14 (35.0)		5 (12.5)	13 (32.5)	22 (55.0)	
	Total (<i>n</i> =105)	80 (76.2)	25 (23.8)		23 (21.9)	36 (34.3)	46 (43.8)	

Low muscle mass is diagnosed by low appendicular skeletal muscle index (ASMI) which defined as <7.0 Kg/m² for men and <5.4 Kg/m² for women. The normal bone mass is defined as *T* value > -1.0SD, osteopenia is defined as -1.0 SD > *T* value > -2.5SD, and osteoporosis is defined as *T* value < -2.5SD.

quantitative computed tomography; the bone material strength index (BMSI) was calculated using a bone indentation osteoprobe. In addition, porosity and low BMSI of the radial cortex have been observed in women with T2DM.¹⁷

In this study, the prevalence rates of osteopenia and osteoporosis in men with HbA1c levels > 9.0% were significantly increased. Compared with patients who had normal BMD, those with osteopenia and osteoporosis had increased HbA1c levels. In a Japanese study, the mean HbA1c had a negative correlation with BMD of the distal radius in both sexes and of the femoral neck in women.¹⁸ A negative correlation between HbA1c levels and calcaneal bone BMD was also found in postmenopausal Chinese women.¹⁹ The prevalence of osteoporosis increases with high levels of blood glucose. Some studies have reported different results. In the Rotterdam study, patients with T2DM and HbA1c > 7.5% had higher BMD and they had a higher BMI compared with participants who did not have diabetes.²⁰ Patients with T2DM usually have greater weight than those without diabetes, which could overestimate BMD values. In our study, participants with osteopenia and osteoporosis had significantly lower weight than those with normal BMD, which may explain why our results were contrary to those of the Rotterdam study. Poor glycemic control increases the risk of fracture in patients with T2DM. In a cohort study among Taiwanese patients with T2DM, the risk of hip fracture among those with HbA1c 9–10% and >10% was significantly higher than that in patients with HbA1c 6–7%.²¹ Bone material

strength in postmenopausal women with T2DM has been negatively correlated with average HbA1c levels over the last 10 years.²²

Bone turnover markers reflect the status of bone turnover and are helpful for the modification of anti-osteoporosis drugs and evaluation of therapy. P1NP is a bone formation marker, whereas B-CTX are bone resorption markers. OC represents the levels of bone turnover (both bone formation and bone resorption levels). We found that patients with T2DM and osteoporosis had higher levels of B-CTX, P1NP, and OC than patients with T2DM who did not have osteoporosis. The high level of bone turnover in patients with T2DM and osteoporosis indicates a reduction in bone mass and increased fracture risk.^{23,24} Our results were similar to those of a previous study.²⁵ A cross-sectional study including 1499 participants found that serum levels of bone turnover markers were negatively correlated with BMD in patients with T2DM.²⁶ Hyperglycemia, gastrointestinal hormone response, microvascular complications, and drug therapy have effects on bone in patients with T2DM. The accumulation of advanced glycation end products (AGEs) in bone causes a non-enzymatic cross-linking of type 1 collagen,²⁷ which affects the material properties of bone. Type 1 collagen modified by AGEs inhibits the differentiation and activity of osteoblasts.²⁸ AGEs also increase the expression of receptor activates transcription factor kappa-B ligand by activating transcription factor nuclear factor-κB (NF-κB) and stimulated interleukin-6 (IL-6) to increase osteoclastic activity.^{29,30}

Table 3. Comparison of various parameters of T2DM patients with differently BMD *T* value.

	Normal	Osteopenia	Osteoporosis	<i>p</i> -value
<i>n</i>	58	71	58	
Age (years)	63.18 ± 7.71	65.14 ± 9.59	65.29 ± 8.66	0.345
Duration of diabetes (years)	13.00 (7.75, 18.00)	12.00 (6.00, 20.00)	12.00 (7.50, 19.00)	0.862
Height (cm)	163.05 ± 7.90	161.34 ± 7.86*	156.60 ± 7.24*.#	0.000
Weight (kg)	71.64 ± 12.02	64.92 ± 9.44*	60.77 ± 8.85*.#	0.000
BMI (kg/m ²)	26.33 ± 4.54	24.92 ± 3.03*	24.83 ± 3.68*	0.052
HbA1c (%)	7.85 (7.18, 8.90)	8.70 (7.10, 10.20)	8.60 (7.20, 9.65)	0.122
Serum creatinine (μmol/l)	57.81 ± 15.49	59.82 ± 14.34*	64.56 ± 14.81*	0.012
BCTX (ng/ml)	0.20 (0.15, 0.29)	0.25 (0.21, 0.34)*	0.32 (0.21, 0.44)*	0.000
OC (ng/ml)	9.00 (7.00, 13.00)	11.00 (9.00, 13.00)	12.00 (9.00, 17.00)*	0.005
P1NP (ng/ml)	27.50 (22.75, 38.25)	34.00 (27.00, 46.50)*	39.00 (32.00, 60.25)*	0.000
25-OH-D (ng/ml)	21.66 ± 6.89	22.23 ± 8.94	19.97 ± 7.93	0.270
Body fat (%)	31.64 ± 9.26	30.48 ± 6.75	32.67 ± 6.35	0.255
ASMI (kg/m ²)	6.91 ± 1.16	6.35 ± 0.85*	6.07 ± 0.84*	0.000
Trunk MM (kg)	23.24 ± 3.88	21.38 ± 3.44*	19.49 ± 2.86*.#	0.000
S/B (%)	59.07 ± 6.42	58.79 ± 6.56	56.97 ± 6.67	0.168
Lumbar spine BMC (g)	72.67 ± 15.43	59.22 ± 11.99*	45.88 ± 9.44*.#	0.000
Femur BMC (g)	38.10 ± 7.60	29.12 ± 7.24*	24.70 ± 5.18*.#	0.000
Lumbar spine BMD (g/cm ²)	1.08 ± 0.12	0.92 ± 0.14*	0.77 ± 0.09*.#	0.000
Femur BMD (g/cm ²)	0.97 ± 0.09	0.82 ± 0.08*	0.74 ± 0.10*.#	0.000

Data are expressed as the mean ± standard deviation or IQR.

*Refers to patients with normal, *p* < 0.05; #Refers to patients with osteopenia, *p* < 0.05.

25-OH-D, 25-hydroxyvitamin D; ASMI, appendicular skeletal muscle index; B-CTX, B collagen specific sequences; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; FBG, fasting plasma glucose; HbA1c, glycated hemoglobin; OC, osteocalcin; P1NP, propeptide of type 1 procollagen; Trunk MM, trunk muscle mass; S/B, the ratio of skeletal muscle mass and body mass; SBP, systolic blood pressure.

The Asian Working Group for Sarcopenia (AWGS) revised the diagnosis of sarcopenia in 2019. It defined three stages of sarcopenia: possible sarcopenia (low muscle strength), sarcopenia (low muscle quality and quantity), and severe sarcopenia (low muscle mass, low muscle strength, and low physical performance).¹⁰ Based on the cutoffs defined by the AWGS, low muscle mass is diagnosed as ASMI < 7.0 kg/m² in men and

< 5.4 kg/m² in women by DXA. Low muscle mass is common in patients with T2DM. In this study, the prevalence rate of low muscle mass was 35.8%, which was higher than the findings in previous research.⁶ The patients with T2DM in this study had poor glycemic control and a long duration of diabetes, with a mean HbA1c level 8.56 ± 1.98% and mean duration 12.84 ± 7.83 years. Low muscle mass was negatively associated with both

Table 4. Multivariable logistic regression analysis of osteopenia/osteoporosis in T2DM patients.

		Osteopenia/osteoporosis		
		OR	(95% CI)	p-value
Male	ASMI	0.422	(0.226–0.787)	0.007
	Age	1.013	(0.952–1.078)	0.675
	HbA1c	1.279	(0.946–1.728)	0.110
	P1NP	1.127	(1.055–1.202)	0.000
Female	ASMI	0.441	(0.223–0.872)	0.019
	Age	1.053	(0.988–1.121)	0.112
	HbA1c	1.192	(0.904–1.570)	0.213
	P1NP	1.009	(0.986–1.033)	0.447

Full results of the logistic regression analyses are shown in Table 4. Adjusted factors were age, height, weight, FBG, HbA1c, body fat, ASMI, BCTX, OC, P1NP, and 25-OH-D.
25-OH-D, 25-hydroxyvitamin D; ASMI, appendicular skeletal muscle index; B-CTX, B collagen specific sequences; CI, confidence interval; FBG, fasting plasma glucose; HbA1c, glycated hemoglobin; OC, osteocalcin; OR, odds ratio; P1NP, propeptide of type 1 procollagen.

disease duration and high HbA1c.^{31,32} We also found that the incidence rate of low muscle mass in women with T2DM whose HbA1c levels were >9.0% was significantly higher than that in patients with HbA1c levels <9.0%. A longitudinal cohort study in Baltimore, USA showed that HbA1c levels could predict the decline in muscle mass and strength.³³ Moreover, the relationship between HbA1c levels and muscle mass was U-shaped; muscle mass was significantly decreased in the highest (>6.1%) and lowest quartiles (<5.5%) of HbA1c levels. Patients with T2DM and HbA1c levels >8.0% had a three to five times higher risk of limited lower extremity access than those with HbA1c levels >5.5%.³⁴ Hyperglycemia contributes to the accelerated decline in muscle mass among patients with T2DM.

Higher blood glucose or HbA1c levels may lead to an increased risk of low muscle mass *via* a variety of mechanisms. The main risk factors are insulin resistance and AGEs. Insulin resistance is a characteristic of T2DM; various inflammatory markers, including IL-6, tumor necrosis factor alpha, and C-reactive protein (CRP) correlate with insulin resistance. Muscle protein metabolism includes muscle protein synthesis and muscle protein breakdown. Muscle protein breakdown is regulated by

inflammatory signaling in the following four main proteolytic pathways: ATP-dependent ubiquitin-proteasome pathway, calpains, macrophage autophagy, and cell apoptosis.³⁵ AGEs are produced *via* the non-enzymatic binding of glucose, proteins, and lipids. They can induce oxidative stress and chronic inflammation, which lead to tissue damage. Skin autofluorescence (AF) is a marker of AGE accumulation in the skin. A cross-sectional study in Japan found that AF in patients with T2DM was negatively correlated with muscle mass and strength.³⁶ In addition, diabetic microangiopathy, peripheral neuropathy, malnutrition, testosterone, and vitamin D deficiency are involved in the decline of muscle mass in T2DM.³⁷ An increase in HbA1c levels leads to the aggravation of blood glucose disorders and the risk of complications. As a result, patients with T2DM are at increased risk of low muscle mass.

Skeletal muscle and bone are anatomically interdependent and interact mechanically and physically. In addition, they can secrete cytokines such as interleukins, prostaglandin (PGE), OC, osteoprotegerin, and receptor activator of NF- κ B. These structures interact with each other *via* paracrine signaling, and PGE2 secreted by bone cells can promote muscle

development. In addition, OC can regulate muscle mass. Adult skeletal muscle expresses myostatin, which may regulate bone density. In a myostatin-deficient mouse model, cortical bone mineral density was increased in the distal femur. In addition, muscle reduction could aggravate insulin resistance and promote the development of T2DM, thereby affecting bone health.³⁸ Low muscle mass is a risk factor for osteoporosis. In the present study, we found that ASMI and trunk muscle mass were significantly decreased in patients with T2DM who had osteopenia and osteoporosis as compared with patients with T2DM and normal BMD. Logistic regression analysis revealed that ASMI was a risk factor for osteopenia and osteoporosis in both men and women. In the 2009–2011 Korean National Health and Nutrition Examination Survey (KNHANES), low muscle mass in men and women was associated with osteoporosis, especially in the femoral neck.³⁹ A cross-sectional study in Finland showed that appendicular muscle mass and femoral neck BMD decreased linearly across menopausal status, with appendicular lean mass declining significantly in late perimenopausal women and BMD declining significantly in postmenopausal women; the decrease of muscle mass precedes that of bone mass in postmenopausal women.⁴⁰ However, patients with osteoporosis are at risk of muscle strength decline.⁴¹ The pathogenesis of low muscle mass and osteoporosis interact with each other and often create a vicious cycle. This process can be aggravated by insulin resistance and chronic inflammation in patients with T2DM; low muscle mass may increase the risk of osteoporosis and fracture in T2DM.

This study had several limitations. Firstly, the number of participants in the study was relatively small. Secondly, we only included participants who were hospitalized; a control group of patients without diabetes was not included. Thirdly, we did not evaluate muscle strength and quality. Fourthly, this was a retrospective cross-sectional study; we did not collect data of participants' diet, physical activity, previous hypoglycemic therapy, menopausal time, and so on. Therefore, further research must be conducted to validate the relationship between low muscle mass and osteoporosis in patients with T2DM, particularly those with worse blood glucose control.

Conclusion

In this study, on the basis of muscle mass and BMD in patients with T2DM and high HbA1c levels, the prevalence rates of low muscle mass in women and the prevalence rates of osteoporosis in men were high with HbA1c > 9%. The ASMI was a risk factor of osteopenia/osteoporosis with T2DM in both men and women. Poor glucose control may increase the prevalence of low muscle mass in women and osteoporosis in men with T2DM.

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Authors' contributions

Lingna Fang: conceptualization, investigation, and original draft of the manuscript; Shao Zhong: methodology; Dan Ma: resources; Chong Li: review, and editing; Yanmin Hao: investigation; Yan Gao: data curation; Li Zhang: resources; Liwen Shen: resources.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Ethics approval and consent to participate

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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