

# A cross-sectional study

## Associations between sarcopenia and clinical characteristics of patients with type 2 diabetes

Mengzhao Cui, MD, Xiaokun Gang, PhD, Gang Wang, MD, Xianchao Xiao, PhD, Zhuo Li, PhD, Zongmiao Jiang, MD, Guixia Wang, PhD\*

### Abstract

Sarcopenia is a geriatric syndrome and it impairs physical function. Patients with type 2 diabetes mellitus (T2DM) are at a higher risk of sarcopenia. The purpose of this study is to explore characteristics of general information and metabolic factors of sarcopenia in patients with T2DM in the northeast of China, and provide information for the prevention and treatment of sarcopenia in clinical practice.

Patients with T2DM aged  $\geq 65$  were recruited in Changchun from March 2017 to February 2018. Questionnaires of general information, physical examination, laboratory and imaging examination were conducted. The patients were assigned into sarcopenia group and non-sarcopenia group according to the diagnostic criteria proposed by Asian working group for sarcopenia (AWGS), and the differences between 2 groups were analyzed.

A total of 132 participants were included in this study, of which, 38 (28.8%) were diagnosed with sarcopenia. 94 (71.2%) were with no sarcopenia. Logistic regression analysis showed that age (OR: 1.182, 95%CI: 1.038–1.346), trunk fat mass (TFM) (OR: 1.499, 95%CI: 1.146–1.960) and free thyroxine (FT4) (OR: 1.342, 95%CI: 1.102–1.635) were independent risk factors for sarcopenia. BMI (body mass index) (OR: 0.365, 95%CI: 0.236–0.661), exercise (OR: 0.016, 95%CI: 0.001–0.169), female (OR: 0.000, 95%CI: 0.00–0.012), metformin (OR: 0.159, 95%CI: 0.026–0.967) and TSM (trunk skeletal muscle mass) (OR: 0.395, 95%CI: 0.236–0.661) were protective factors for sarcopenia.

Sarcopenia in patients with T2DM is associated with increased age, increased TFM and increased FT4 level. Regular exercise, female, metformin administrations, high BMI and increased TSM are associated with lower risk of sarcopenia.

**Abbreviations:** AFM = appendicular fat mass, AGEs = advanced glycation end products, ASM = appendicular skeletal muscle mass, ASMI = appendicular skeletal muscle mass index, AWGS = Asian working group for sarcopenia, BMD = bone mineral density, BMI = body mass index, CRP = c-reactive protein, DXA = dual energy X-ray absorptiometry, FBG = fasting blood glucose, Fins = fasting insulin, FT4 = free thyroxine, H = height, HDL = high density lipoprotein, PTH = parathyroid hormone, T2DM = type 2 diabetes mellitus, TFM = trunk fat mass, TSM = trunk skeletal muscle mass.

**Keywords:** clinical characteristics, diabetes mellitus, type 2, sarcopenia

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethics committee of the First Hospital of Jilin University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The authors declare that they have no conflict of interest.

Department of Endocrinology and Metabolism of the First Hospital of Jilin University, Changchun, Jilin Province, China.

\* Correspondence: Guixia Wang, Department of Endocrinology and Metabolism of the First Hospital of Jilin University, NO 71. Xinmin Street, Changchun, Jilin Province, China (e-mail: gwang168@jlu.edu.cn).

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### 1. Introduction

The musculoskeletal system plays an important role in maintaining posture, completing movements, protecting vital internal organs, and maintaining homeostasis of the body. As aging, musculoskeletal disease has become a serious public health issue. Sarcopenia is a geriatric syndrome, which is associated with age. It is characterized by the reduce of muscle mass, decrease of muscle strength and decline of physical performance.<sup>[1]</sup> It is related to reduced physical ability, impaired cardio-respiratory function, disability and death in the elderly.<sup>[2]</sup> The age-related reduction of muscle mass is mainly a reduction of type II muscle fibers and motor neurons and infiltration of muscle lipid.<sup>[3]</sup> Sarcopenia not only affects daily activities of the elderly resulting in the decline of the quality of life, but also accelerates the progress of metabolic diseases. It is estimated that 50 million people worldwide are suffering from sarcopenia nowadays, and the number will rise to 500 million by 2050,<sup>[4]</sup> indicating that sarcopenia will increase the burden of social medical expenses, raising concern worldwide.

The definition and diagnostic criteria of sarcopenia proposed by AWGS,<sup>[1]</sup> adequately covers the body composition, genetic background and ethnicity of Asian people. According to the diagnostic criteria of AWGS, the prevalence of sarcopenia is between 6.8% and 31%,<sup>[5–8]</sup> which is related to a variety of factors, including gender, age, hormone level, BMI, inflammatory

markers, T2DM and tumor.<sup>[6,9,10]</sup> Patients with T2DM are at a higher risk in developing sarcopenia.<sup>[11]</sup> Changes of the muscular fibers in participants with T2DM may be due to diabetic complications and insulin resistance. Possible mechanism could be oxidative type I muscular fibers reduced and glycolytic type II fibers increased,<sup>[12]</sup> which accelerate the declination of muscle mass and strength. Furthermore, sustained hyperglycemia increases the accumulation of advanced glycation end products (AGEs) in the muscles and cartilage, which in return leads to muscle stiffness and reduced muscle function.<sup>[13,14]</sup>

According to AWGS, there were some studies on sarcopenia conducted in the southern districts of China, but none has been reported in the north. Since there are differences in lifestyles including diet and exercise et al, as well as climate between south and north, this study aims to first demonstrate the clinical characteristics of sarcopenia in T2DM in the northeast of China and discuss the factors associated with sarcopenia, in order to provide the evidence for possible effective preventions and treatments.

## 2. Methods

### 2.1. Subjects

A cross-sectional study was conducted during March, 2017 to February, 2018 in the department of endocrinology and metabolism of the First Hospital of Jilin University. In-patients at the department who aged  $\geq 65$  and met the diagnostic criteria of T2DM proposed by WHO in 1999 were recruited. The participants received at least half an hour of sunlight daily (self-reported). All the participants signed informed consent designed by ethical board of the First Hospital of Jilin University. Participants who had severe peripheral neuropathy, disuse muscle atrophy, malignant tumor, severe cognitive disorder, autoimmune disease were excluded from the study. Participants who had supplement of Vitamin D, medications affecting skeletal muscle in the last 3 months were also excluded from the study. Participants who remained long-term bedridden, and/or failed to complete dual-energy X-ray absorptiometry (DXA), were excluded. The study complied with the Declaration of Helsinki, and was approved by the ethics committee of the First Hospital of Jilin University.

### 2.2. Questionnaires

Questionnaires were self-reported, and the followings were included:

- (1) general conditions of each subject including name, gender, nation, age, menstrual and obstetrical histories, educational level, occupation, type of medical insurance, smoking and alcoholism history.
- (2) daily exercise (type, duration and frequency), sleep (time and duration), diet and history of tumbles.
- (3) medical history including hypertension, coronary artery disease, cerebrovascular disease and duration history of diabetes, application of anti-diabetic drugs (type, dose, frequency) and subcutaneous insulin (type, dose, frequency).

### 2.3. Anthropometric measurements

- (1) Height and weight were measured according to the clinical standard.

- (2) BMI was calculated by dividing weight (in kilograms) by the square of the height (in meters).
- (3) Step speed was calculated as the time taken for 6 meters' walk divided by 6 meters. The participants walked at daily speed. Record the time with a stopwatch (accurate to 0.01 seconds). The average values were calculated after a second measurement.
- (4) Grip dynamometer (EH-101 electronic dynamometer, China) was used to measure the grip strength of the dominant hand for 3 times, and the maximum grip strength value was taken into analysis.
- (5) Calf circumference was measured around the most prominent part of the gastrocnemius muscle (accurate to 0.1 cm). We asked the participants to stand with their feet shoulder-width apart. Average values were obtained after measuring the left and right sides respectively.

### 2.4. Body composition by DXA

Measuring instrument: Dual-Energy X-ray Absorptiometry (Luna Prodigy Advance, GE, America).

Measurement method: total body muscle mass, fat mass of the participants was measured, and the CV value of muscle content was 0.89%. All the above measurements were performed by the same technician. Appendicular skeletal muscle mass index (ASMI) = [Appendicular skeletal muscle mass (ASM) (kg)/Height (H)<sup>2</sup> (m<sup>2</sup>)]. ASMI is a diagnostic indicator of reduced skeletal muscle mass.

Diagnosis of sarcopenia: according to AWGS, the diagnostic criteria<sup>[11]</sup> is defined as the following: the cut-off of reduction of muscle mass is that ASMI is less than 7.0 kg/m<sup>2</sup> (male) and 5.4 kg/m<sup>2</sup> (female), together with weakness of muscle strength (less than 26.0 kg (male), less than 18.0 kg (female)) and (or) decline of step speed (less than 0.8 m/seconds).

### 2.5. Biochemical measurements

Eight-hour fasting samples were collected for each participant. Blood samples were centrifuged at 3000 rpm for 8 minutes at 4°C, aliquoted to yield serum and plasma and then stored at -80°C until analyses. Fasting blood glucose (FBG), post-prandial glycemia, liver function, renal function, serum lipid, and creatine kinase were determined by colorimetry (7600-210, Hitachi). Glycosylated hemoglobin was determined by multi-effect liquid chromatography (BIO-RAD-VARIANT2). Blood routine was determined by Semiconductor laser nucleic acid staining method (Sysmex XN9000-1). Thyroid function, 0-minute C peptide and fasting insulin (Fins) were determined by electro-chemiluminescence method (Cobas e62, Roche). HOMA-IR (calculation formula = FBG (mmol/L)\*Fins (mU/L)/22.5). 8:00 blood cortisol, testosterone (male), estradiol (female) and parathyroid hormone (PTH) were determined by chemiluminescence method (DXI800, Bechman). 25-OH-vitamin D and 25-OH-vitamin D3 were measured by liquid chromatography tandem mass spectrometry. C-reactive protein (CRP) was determined by turbidimetry method (7600-210, Hitachi). Twenty-four-hours urinary protein and 24-hours micro albumin were determined by immunoturbidimetry method (7600-210, Hitachi). And lower limb artery ultrasound, carotid ultrasound, sensory nerve quantitative examination, fundus examination and systemic bone mineral density (BMD) were performed successively.

**Table 1**  
**Characteristics of subjects categorized by groups of sarcopenia.**

	Sarcopenia (n=38)	Non-sarcopenia (n=94)	P
Gender (male/female)	21 (55.3)/17 (44.7)	38 (40.4)/56 (59.6)	.121
Age (years)	73.5 (68,77.25)	68 (65,72)	.000*
Duration of diabetes (years)	14.0 (5.0,22.0)	13.0 (8.0,18.0)	.590
History of hypertension	22 (57.9)	54 (57.4)	.962
History of coronary heart disease	13 (34.2)	29 (30.9)	.708
History of cerebrovascular disease	10 (26.3)	14 (14.9)	.123
Smoking	10 (26.3)	24 (25.5)	.926
Drinking	6 (15.8)	12 (12.8)	.647
Snoring	16 (42.1)	62 (66.0)	.012*
Exercise	20 (52.6)	65 (69.1)	.073
High-protein diet	11 (28.9)	37 (39.4)	.260
History of fall	12 (31.6)	18 (19.1)	.123
ASM (kg) <sup>†</sup>	16.42 (13.06,19.26)	17.65 (15.76,22.58)	.001*
ASM/H <sup>2</sup> (kg/m <sup>2</sup> )	5.67 (5.02,6.63)	6.90 (6.18,7.71)	.000*
AFM (kg) <sup>‡</sup>	6.21 (4.45,7.70)	7.35 (5.44,8.66)	.013*
TSM (kg) <sup>§</sup>	20.99±3.17	23.46±3.86	.001*
TFM (kg) <sup>  </sup>	11.56±4.27	14.55±4.69	.001*
BMI (kg/m <sup>2</sup> )	22.86±2.71	26.34±3.35	.000*

\* Significantly different;

<sup>†</sup> appendicular skeletal muscle mass;

<sup>‡</sup> appendicular fat mass;

<sup>§</sup> trunk skeletal muscle mass;

<sup>||</sup> trunk fat mass.

## 2.6. Statistical analysis

Statistical analyses were performed using SPSS 24.0 software. Data are presented as mean ± SD or median (interquartile range). In all cases, probability (*P*) value of <.05 was considered statistically significant. The *t* test was used to determine differences in various parameters between 2 groups. Frequencies were compared between 2 groups by Fisher exact test. The associations between sarcopenia and clinical characteristics were assessed by logistic regression analysis.

## 3. Results

### 3.1. Characteristics of participants grouped by sarcopenia

A total of 132 (59 males and 73 females) participants were included in this study. As shown in Table 1, 38 participants were diagnosed with sarcopenia, accounting for 28.8%, with an average age of 73.5 years, and 94 had no sarcopenia, accounting for 71.2%, with an average age of 68 years. The average age of the sarcopenia group was higher than that of the non-sarcopenia group (*P* < .05), and participants from the sarcopenia group had lower BMI, ASM, ASM/H<sup>2</sup>, appendicular fat mass (AFM), TSM

and TFM than those of the non-sarcopenia group (*P* < .05). Interestingly, sarcopenia group tends to snore less than non-sarcopenia during sleep (*P* < .05). No significant difference were found in gender, duration of diabetes, history of hypertension, history of coronary heart disease, history of cerebrovascular disease, smoking, drinking, exercise, high-protein diet, and history of tumbles between 2 groups (*P* > .05).

### 3.2. The distribution of age and gender

The overall prevalence of sarcopenia was 28.8%, and the prevalence was 35.6% in male and 23.3% in female (*P* > .05). Grouped by age, as shown in Table 2, the prevalence of sarcopenia in each age group was 17.4%, 28.1%, 52.4%, 60%, respectively (*P* < .001). And the prevalence of sarcopenia increased with age (*P* < .001). Grouped by gender, the prevalence of sarcopenia in women of all age groups was 15.0%, 20.0%, 36.4%, and 57.1%, respectively, with no significant difference (*P* > .05). The prevalence of sarcopenia in men in all age groups was 20.1%, 35.3%, 70.0%, 66.7%, respectively (*P* < .05). Moreover, the prevalence of sarcopenia increased with age in men (*P* < .05), and the trend was shown in Figure 1.

### 3.3. Sarcopenia and indicators related to diabetes

According to the duration of diabetes, the participants were subdivided into 3 groups, 10 years and below group, 10 to 20 years group and 20 years above group, as shown in Table 3. The prevalence of sarcopenia was 27.6%, 21.8%, and 52.6%, respectively (*P* < .05). Participants in 20 years above group had significantly higher prevalence of sarcopenia than the other 2 groups (*P* < .05).

The number of participants who received metformin treatment in the sarcopenia group was significantly fewer than those in the non-sarcopenia group (*P* < .05). In addition, 36 of the participants did not use exogenous insulin, and their fasting insulin and HOMA-IR in the sarcopenia group were all significantly lower than those in the non-sarcopenia group (*P* < .05). No significant difference in fasting blood glucose, 2-hour postprandial blood glucose, glycosylated hemoglobin, 0-minute C peptide, diabetic retinopathy, diabetic peripheral neuropathy, whether to use hypoglycemic agents, and whether to use exogenous insulin between sarcopenia and non-sarcopenia groups (*P* > .05) (Table 4).

### 3.4. Sarcopenia and biochemical indicators, hormonal indicators

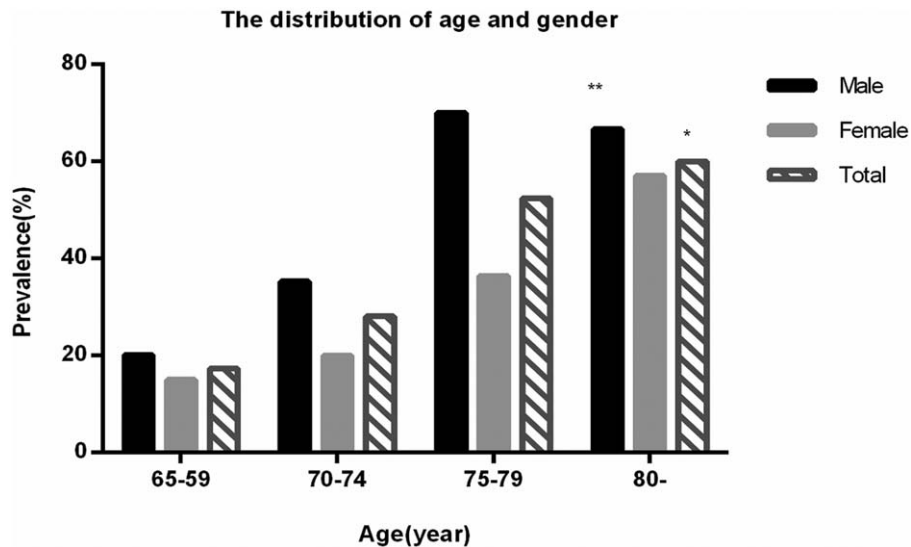
As shown in Table 5, serum uric acid and triglycerides of the sarcopenia group were both significantly lower than those of the non-sarcopenia group (*P* < .05). FT4 in the sarcopenia group was

**Table 2**  
**The distribution of age and gender.**

Age	Total number	Total number of sarcopenia n (%)	Total number of females n	Number of female patients n (%)	Total number of males N	Number of male patients n (%)	P
65–69	69	12 (17.4)	40	6 (15.0)	29	6 (20.1)	.538
70–74	32	9 (28.1)	15	3 (20.0)	17	6 (35.3)	.444
75–79	21	11 (52.4)	11	4 (36.4)	10	7 (70.0)	.198
80 and above	10	6 (60.0) <sup>*</sup>	7	4 (57.1)	3	2 (66.7) <sup>†</sup>	1.000

\* Prevalence of sarcopenia in all age groups was compared in overall patients, Pearson chi-square=14.154, *P*=.003; Pearson chi-square of trend test=14.177, *P*=.000.

<sup>†</sup> Prevalence of sarcopenia in all ages was compared in men, Pearson chi-square=7.863, *P*=.036; Pearson chi-square of trend test=7.413, *P*=.006.



**Figure 1.** The distribution of age and gender. \*The prevalence of sarcopenia in each age group was significantly different, and the prevalence of sarcopenia increased with age ( $P < .001$ ). \*\*The prevalence of sarcopenia in men of all age groups was significantly different, and it increased with age in men ( $P < .05$ ).

significantly higher than that in the non-sarcopenia group ( $P < .05$ ). The T-value of systemic BMD in the sarcopenia group was significantly lower than that in the non-sarcopenia group ( $P < .05$ ). As shown in Table 6, the subjects were assigned into normal triglyceride group (0.28–1.8 mmol/L) and triglyceride-

elevated group ( $>1.8$  mmol/L), and the prevalence of sarcopenia was, 39.7% and 15.3%, respectively ( $P < .05$ ).

### 3.5. Sarcopenia and physical examination

**3.5.1. Sarcopenia and BMI.** The subjects were sub-divided into 4 groups, those are, the underweight group ( $\text{BMI} < 18.5 \text{ kg/m}^2$ ), the normal weight group ( $18.5\text{--}23.9 \text{ kg/m}^2$ ), the overweight

**Table 3**

Prevalence of sarcopenia in different durations of diabetes.

Durations of diabetes	Sarcopenia n (%)	Non-sarcopenia n (%)	P
10 yr and below	16 (27.6)*	42 (72.4)	.037
10–20 yr	12 (21.8)†	43 (78.2)	
20 yr above	10 (52.6)	9 (47.4)	

\* Comparison between 10 yr and below group and 20 yr above group, Pearson chi-square = 4.014,  $P = .045$ , OR: 2.917, 95%CI: 1.002, 8.494;

† Comparison between 10 and 20 yr group and 20 yr above group, Pearson chi-square = 16.293,  $P = .000$ , OR: 3.981, 95%CI: 1.999, 7.932.

**Table 4**

Related indicators of diabetes in sarcopenia and non-sarcopenia groups.

	Sarcopenia n (%)	Non-sarcopenia n (%)	P
Antidiabetic drug	22 (57.9)	61 (64.9)	.451
Metformin	5 (13.2)	39 (41.5)	.002*
Exogenous insulin	26 (68.4)	70 (74.5)	.480
Fasting blood glucose (mmol/L)	7.83 (5.84, 10.03)	8.21 (6.56, 10.95)	.457
2-hour postprandial blood glucose (mmol/L)	14.43 ± 4.67	14.82 ± 3.97	.628
Glycosylated hemoglobin (%)	7.5 (6.9, 10.1)	8.1 (7.1, 9.6)	.771
0-minute C peptide (nmol/L)	0.59 (0.38, 0.81)	0.65 (0.49, 0.88)	.126
Diabetic retinopathy	11 (28.9)	29 (30.9)	.829
Diabetic peripheral neuropathy	28 (73.7)	63 (67.0)	.454
Fasting insulin (pmol/L)	44.63 (25.13, 74.97)	109.95 (59.02, 137.08)	.004*
HOMA-IR	2.71 (1.75, 3.11)	5.94 (3.71, 8.91)	.002*

\* Significantly different.

**Table 5**

Biochemical indicators and hormonal indicators of the sarcopenia and non-sarcopenia groups.

Indicators	Sarcopenia	Non-sarcopenia	P
Albumin (g/L)	38.15 (34.53, 42.23)	39.80 (37.88, 42.40)	.078
Blood urea nitrogen (nmol/L)	6.51 (5.10, 7.34)	6.76 (5.35, 7.94)	.207
Creatinine ( $\mu\text{mol/L}$ )	66.65 (56.25, 75.70)	70.95 (57.10, 80.78)	.218
Cystatin C (mg/L)	0.93 (0.82, 1.12)	0.89 (0.81, 1.01)	.343
Serum uric acid (mmol/L)	200.53 ± 81.74	333.06 ± 81.99	.041*
Total cholesterol (mmol/L)	4.52 (3.97, 5.20)	4.88 (4.07, 5.65)	.128
Triglyceride (mmol/L)	1.34 (1.02, 1.76)	1.84 (1.32, 2.46)	.001*
LDLC (mmol/L)	2.82 ± 0.77	2.97 ± 0.88	.340
HDLC (mmol/L)	1.24 ± 0.28	1.23 ± 0.35	.863
Creatine kinase (U/L)	74 (55, 118)	86 (70, 123)	.097
TSH (uIU/mL)	2.08 (1.10, 2.97)	2.37 (1.50, 4.06)	.120
FT3 (pmol/L)	4.32 (3.68, 4.75)	4.43 (3.97, 4.89)	.153
FT4 (pmol/L)	16.44 (14.07, 18.87)	14.98 (13.70, 16.56)	.024*
8:00 Blood cortisol (nmol/L)	323.44 ± 76.54	294.72 ± 91.24	.090
Testosterone (nmol/L)	10.01 ± 4.28	10.78 ± 5.03	.691
PTH (pg/mL)	38.60 (29.60, 46.83)	39.85 (29.90, 50.85)	.557
25-OH-Vitamin D (ng/mL)	19.43 ± 10.38	18.79 ± 7.22	.686
25-OH-Vitamin D3 (ng/mL)	18.01 ± 10.32	16.43 ± 7.19	.319
CRP (mg/L)	3.02 (3.02, 3.13)	3.02 (3.02, 3.86)	.516
24-h urinary protein (g/24 h)	0.28 (0.20, 0.37)	0.26 (0.20, 0.40)	.566
24-h micro albumin (mg/24 h)	23.61 (10.90, 96.59)	18.96 (10.90, 63.33)	.925
T value of systemic BMD	-0.876 ± 1.18	-0.249 ± 1.36	.014*

BMD = bone mineral density, CRP = c-reactive protein, FT3 = free triiodothyronine, FT4 = free thyroxine, HDLC = high density lipoprotein cholesterol, LDLC = low density lipoprotein cholesterol, PTH = parathyroid hormone, TSH = thyroid stimulating hormone.

\* Significantly different.



**Table 6**  
**Prevalence of sarcopenia in different triglyceride group.**

Triglyceride (mmol/L)	Sarcopenia n (%)	Non-sarcopenia n (%)	P
Normal group (0.28–1.8)	29 (39.7)	44 (60.3)	.001*
Elevated group (>1.8)	9 (15.3)	50 (84.7)	

\*Significantly different.

**Table 7**  
**Prevalence of sarcopenia in different BMI groups.**

BMI (kg/m <sup>2</sup> )	Sarcopenia n (%)	Non-sarcopenia n (%)	P
Underweight (<18.5)	3 (100)	0 (0)	.000*
Normal weight (18.5–23.9)	23 (53.5)	20 (46.5)	
Overweight (24.0–27.9)	11 (19.3)	46 (80.7)	
Obesity (≥28.0)	1 (3.4)	28 (96.6)	

\*Prevalence of sarcopenia in all BMI groups was compared, Pearson chi-square=31.38, P=.000; Pearson chi-square of trend test=29.58, P=.000.

group (24.0–27.9 kg/m<sup>2</sup>) and the obesity group (>28.0 kg/m<sup>2</sup>). As shown in Table 7, the prevalence of sarcopenia of each group was significantly different (P<.001). Moreover, with BMI level increasing, the prevalence of sarcopenia significantly decreased (P<.001), as shown in Figure 2.

**3.5.2. Sarcopenia and grip strength, calf circumference.** Stratified by gender, grip strength of men and women in sarcopenia group were both significantly lower than that of non-sarcopenia group (P<.001), and calf circumference of men and women in sarcopenia group was both significantly lower than that in non-sarcopenia group (P<.001), as shown in Table 8.

**3.6. Logistic multiple regression analysis of influence factors for sarcopenia**

Logistic multiple regression analysis showed that age (OR: 1.182, 95%CI: 1.038–1.346), TFM (OR: 1.499, 95%CI: 1.146–1.960)

**Table 8**  
**Grip strength and calf circumference stratified by gender.**

Indicators	Layers	Sarcopenia	Non-sarcopenia	P
Grip strength (kg)	male	26.01±6.36	31.18±6.43	.004*
	female	14.8 (13.1,17.8)	19.7 (17.3,22.1)	.000*
Calf circumference (cm)	male	34.0 (33.0,36.0)	36.1 (35.0,37.5)	.000*
	female	32.5 (31.0,34.0)	35.2 (33.5,36.0)	.000*

\*Significantly different.

**Table 9**  
**Logistic multiple regression analysis of influence factors for sarcopenia.**

Variable	β	SE	Wald χ <sup>2</sup>	P	OR	95%CI
Age	0.167	0.066	6.393	.011	1.182	1.038–1.346
TFM	0.405	0.137	8.724	.003	1.499	1.146–1.960
FT4	0.294	0.101	8.562	.003	1.342	1.102–1.635
BMI	-1.009	0.299	11.395	.001	0.365	0.236–0.661
Exercise	-4.147	1.210	11.753	.001	0.016	0.001–0.169
Gender	-8.873	2.287	15.060	.000	0.000	0.00–0.012
Metformin	-1.839	0.921	3.985	.046	0.159	0.026–0.967
TSM	-0.928	0.263	12.490	.000	0.395	0.236–0.661

and FT4 (OR: 1.342, 95%CI: 1.102–1.635) were independent risk factors for sarcopenia. BMI (OR: 0.365, 95%CI: 0.236–0.661), exercise (OR: 0.016, 95%CI: 0.001–0.169), female (OR: 0.000, 95%CI: 0.00–0.012), metformin (OR: 0.159, 95%CI: 0.026–0.967) and TSM (OR: 0.395, 95%CI: 0.236–0.661) were protective factors for sarcopenia, as shown in Table 9.

**4. Discussion**

According to previous literatures, sarcopenia in patients with T2DM are at a higher risk of sarcopenia, which lead the current study focusing on sarcopenia in patients with T2DM. A study conducted in China has reported that participants with T2DM have 1.56 times higher risk of sarcopenia than healthy people.<sup>[15]</sup>

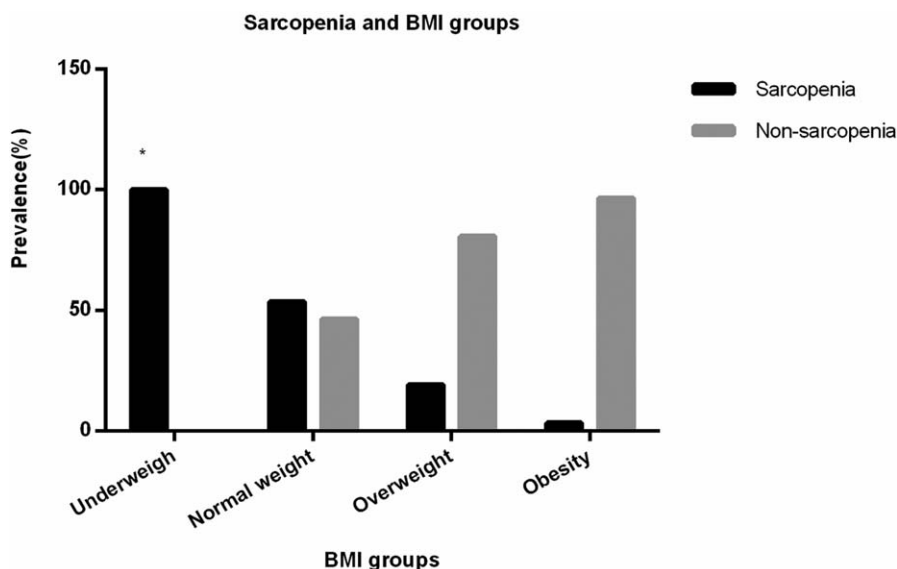


Figure 2. Sarcopenia and BMI groups. \*With BMI level increasing, the prevalence of sarcopenia significantly decreased (P<.001).

A Korean researcher has reported<sup>[16]</sup> that the risk of reduction of muscle mass increases 2 to 4 times in participants with T2DM. On one hand, insulin stimulates protein synthesis, insufficient secretion of insulin or insulin resistance will lead to insufficient muscle protein synthesis and increased protein degradation, which may result in sarcopenia.<sup>[17]</sup> On the other hand, persistent hyperglycemia causes AGEs to accumulate in muscles and cartilages, leading to muscle stiffness and dysfunction.<sup>[13,14]</sup> AGEs also promote inflammation and dysfunction of endothelial cells in microcirculation of skeletal muscles through receptors of AGEs, which lead to sarcopenia.<sup>[18]</sup> T2DM patients with increased levels of cytokines such as TNF and IL-6 show negative effects on muscle mass and function.<sup>[19]</sup> Other studies have demonstrate that hyperglycemia causes decline of muscle function in the early stages of T2DM, and diabetic peripheral neuropathy accelerates the progress of sarcopenia in the late stage.<sup>[20]</sup> In return, with the development of sarcopenia, mobility of the elderly declines, the muscle's intake of glucose reduces, insulin resistance increases, and diabetes, therefore, will progress. Therefore, the relationship between sarcopenia and T2DM is obvious and we analyzed the clinical characteristics of sarcopenia in T2DM.

#### 4.1. Sarcopenia and indicators related to diabetes in T2DM

This study showed that the prevalence of sarcopenia was significantly higher in the group with a diabetic duration over 20 years than the other 2 groups. This result suggests that the long course of diabetes may promote the occurrence and development of sarcopenia, but the mechanism is not clear yet. Kalyani et al<sup>[20]</sup> have reported that the prevalence of sarcopenia in T2DM combined with chronic complications including renal insufficiency and (or) peripheral neuropathy may be higher than those without complication. This suggests the longer the course of diabetes, the higher the prevalence of chronic complications, the higher risk of sarcopenia occurs, which is consistent with current findings. However, no clear relationship between sarcopenia and diabetic complications were found in this study, considering the severity of diabetic peripheral neuropathy is not sensible by quantitative sensory testing, which may cause misunderstanding in the results.

As for insulin resistance, since the skeletal muscle is one of the main organs that insulin acts on, the loss of muscle mass can negatively regulate the body's sensitivity to insulin, which contributes to the progress of insulin resistance. This study showed that fasting insulin was lower in sarcopenia group, suggesting reduction of endogenous secretion of insulin may be associated with sarcopenia. It is related to the worse function of pancreatic  $\beta$  cells in older people and in patients with long duration of diabetes, which leads to failure in stimulating the synthesis of muscle proteins. Shishikura et al<sup>[21]</sup> have reported decreased insulin secretion was associated with reduced muscle mass, and another study showed deficient insulin secretion was a risk factor in men with T2DM,<sup>[22]</sup> which were consistent with our results. Previous studies<sup>[12,23]</sup> have demonstrated insulin resistance is associated with sarcopenia, however, current study showed that HOMA-IR in the sarcopenia group was significantly lower than that in the control group, which was probably due to the influence of confounding factors such as weight, BMI and abdominal circumference, and these results require further investigation.

This research showed that the number of participants taking metformin in sarcopenia group was significantly fewer than that in non-sarcopenia group. A randomized, controlled trial involving 91 non-diabetic participants has revealed<sup>[24]</sup> that gait speed improved in the group of participants who were regularly taking metformin treatment than those who did not, most likely due to the administration of metformin may improve insulin resistant, also due to the increased uptake of glucose and calcium in skeletal muscles,<sup>[25]</sup> as well as inhibition of inflammation and oxidative stress levels. Metformin is an AMPK agonist, which can enhance the insulin's reaction in adult tissues. Activation of AMPK is also related to autophagy, thus metformin can lead to the induction of atrophic gene MurF1 because of autophagic cell death.<sup>[26]</sup> However, no study has shown that metformin leads to atrophy of skeletal muscles *in vivo*,<sup>[27]</sup> which needs further study.

#### 4.2. Sarcopenia and gender in T2DM

This study showed that prevalence of sarcopenia was 35.6% in men and 23.3% in women. The single factor analysis indicated no significant difference between gender. But the logistic regression analysis suggested that male participants were more likely to suffer from sarcopenia than female participants. The mechanism by which skeletal muscle mass of males decreases faster than that of females remains unclear, but it may be related to the decrease in testosterone secretion. Verschueren et al have suggested that testosterone promotes the synthesis of muscle protein, which is more significant in maintaining muscle mass and muscle function than estrogen,<sup>[28]</sup> but after the age of 30, testosterone levels in males decrease by 1% per year. Both in human and rodent studies, androgens induce a great increase in muscle mass.<sup>[29]</sup>

#### 4.3. Sarcopenia and age in T2DM

Our study showed the prevalence of sarcopenia in different ages was significantly different and it increased with age. Moreover, logistic regression presented that age was an independent risk factor for sarcopenia, suggesting that more attentions are needed to elder people. Age-related decline in exercise capacity is a major factor in the decline of muscle mass and muscle strength in older adults.<sup>[30]</sup> Studies showed that muscle mass declines after peaking in the fourth decade, and after the age of 70, the loss of motor neurons can reach up to 50%, which significantly affects functions of lower limbs,<sup>[23]</sup> which are consistent with current findings.

#### 4.4. Sarcopenia and exercise in T2DM

Studies have shown that sedentary behavior results in loss of muscle mass, while exercise, due to its anabolic effect, can fight against sarcopenia mainly through different mechanisms, activation of mTORC1 reducing the expression of pro-inflammatory mediators and oxidative stress, and increasing mitochondrial synthesis and tissue reactivity to insulin.<sup>[31,32]</sup> Resistance exercise is the best choice for the prevention and control of sarcopenia, which can promote the synthesis of net muscle proteins, increase muscle mass, muscle strength and muscle quality, while aerobic exercise is more suitable for maintaining and increasing cardiovascular fitness.<sup>[31]</sup> In this study, multi-factor logistic regression analysis showed that

exercise was a protective factor for sarcopenia, and aerobic exercise or resistance exercise was not distinguished, but mostly aerobic exercise. Chronic aerobic exercise has significant influences on mitochondria, reducing mitochondrial apoptosis and enhancing mitochondrial biosynthesis. Therefore, the elder people should be encouraged to do aerobic and resistance exercise appropriately.

#### 4.5. Sarcopenia and metabolism in T2DM

This study suggested that patients in sarcopenia group had a lower BMI, which was consistent with the previous study,<sup>[9]</sup> indicating the loss of muscle mass may cause loss of weight. Asians tend to have a relative lower weight than Caucasians, and Asians rarely show sarcopenic obesity. In addition, the calf circumference of both men and women in the sarcopenia group was significantly lower than that of the non-sarcopenia group. Regarding trunk fat mass, this study showed that TFM was an independent risk factor, which might be related to abdominal obesity and increased visceral fat. Adipose tissues increase the secretion of inflammatory markers and lead to the occurrence of sarcopenia.

In the present study, the serum uric acid in the sarcopenia group was significantly lower than that in the non-sarcopenia group. Serum uric acid decreases the level of NO in endothelial cells, thereby, increasing the blood flow of skeletal muscle and glucose uptake, and is also associated with the activity of insulin.<sup>[33]</sup> Uric acid in proper level acts as a powerful antioxidant and a scavenger of singlet oxygen and free radicals. Uric acid may protect the proteins from oxidative damage due to the antioxidant capacity.

The current study showed that the risk of sarcopenia was significantly higher in the normal triglyceride group than in the triglyceride-elevated group. Since sarcopenia group presented lower ASM, AFM, TSM, TFM, and BMI and may be not sufficient in nutrient, it is easy to conclude. A Korean study<sup>[34]</sup> has reported that, when using ASM/weight as the diagnostic index, elderly men with sarcopenic obesity are at a higher risk of dyslipidemia than those with sarcopenia alone or simple obesity. Another study<sup>[35]</sup> has indicated that among postmenopausal women, those who are purely obese had higher triglycerides and lower high density lipoprotein (HDL) cholesterol than those with sarcopenic obesity. In our study, ASM/H<sup>2</sup> was used as the diagnostic indicator of sarcopenia, since the definition of sarcopenia varies, the results may be different.

In addition, the loss of muscle mass in participants with sarcopenia may indeed cause low metabolic level of the body, leading to low calf circumference, low BMI, low serum uric acid and low triglyceride. Moreover, this study is a cross-sectional study, which cannot distinguish the cause and effect of the 2 factors. Therefore, further prospective studies are needed to clarify the cause and effect of the 2 factors.

#### 4.6. Sarcopenia and hormones in T2DM

This study presented that FT4 was a risk factor for sarcopenia, suggesting higher FT4 levels may be associated with sarcopenia. A study by Van et al<sup>[36]</sup> has indicated that increased FT4 level is associated with decreased physical performance and muscle strength, independent of TSH levels. In addition, hyperthyroidism is associated with weight loss, while exercise capacity and loss of weight are both signs of frailty and are similar to sarcopenia.

Besides, this study showed that *T* value of systemic body bone mineral density in sarcopenia group was lower than that of the non-sarcopenia group, while the *T* value of systemic BMD could not substitute for *T* value of lumbar or femoral BMD. However, to some extent, it demonstrated that the bone mass was positively correlated with muscle mass. There was a positive correlation between the regulation of muscle mass and bone mass in elder participants. Since both myoblasts and osteoblasts originate from pluripotent mesenchymal stem cells, muscles and bones are regulated by some of the same genes. The study of GWAS suggested that the coding genes of myostatin,  $\alpha$ -actinin 3, etc were closely related to both sarcopenia and osteoporosis.<sup>[37]</sup>

#### 4.7. Limitations and prospects

Firstly, this is a cross-sectional study, which limits its cause-and-effect conclusion. Secondly, the sample size included in this study was relatively small, the researchers are planning to increase the sample size in future studies. In addition, prospective study can be carried out for the study of sarcopenia in 3 aspects respectively, the influence factors of muscle mass, muscle strength and physical performance. In conclusion, the risk of sarcopenia in participants with T2DM is associated with aging, increased trunk fat mass and increased FT4 level. Regular exercise, female, metformin administrations, high BMI and increased TSM are associated with low risk of sarcopenia.

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#### Author contributions

**Conceptualization:** Guixia Wang.

**Data curation:** Xiaokun Gang.

**Formal analysis:** Zhuo Li.

**Funding acquisition:** Guixia Wang.

**Investigation:** Mengzhao Cui.

**Methodology:** Xiaokun Gang.

**Project administration:** Gang Wang, Xianchao Xiao, Zongmiao Jiang.

**Validation:** Xianchao Xiao.

**Writing – original draft:** Mengzhao Cui, Xiaokun Gang.

**Writing – review & editing:** Guixia Wang, Xiaokun Gang.

Guixia Wang orcid: 0000-0001-8107-616X.

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