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Association between sarcopenia and the foot-ankle function in type 2 diabetic foot ulcer

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Abstract

Background The diabetic foot (DF) ulcer is the severe complication of type 2 diabetes mellitus (T2DM). Sarcopenia is characterized as the loss of muscle mass and strength, resulting in the increased risk of fracture and physical disability. Sarcopenia may affect the foot-ankle function in DF ulcer patients, compromise the quality of life.

Objective The aim was to clarify the effect of sarcopenia on foot-ankle function in patients with DF ulcer.

Methods In total of 108 T2DM patients with DF ulcer were enrolled. Based on the examination of muscle mass by dual energy X-ray absorptiometry (DXA) and grip strength and 5x sit-to-stand test, the DF patients were divided into sarcopenia and non-sarcopenia groups. The severity of DF ulcer was evaluated by Wagner classification. The foot-ankle function was evaluated by American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score.

Results DF patients with sarcopenia showed advanced age, lower BMI, longer duration of T2DM, and more severe Wagner classification, reduced appendicular skeletal muscle mass index (ASMI), grip strength, transcutaneous oxygenpressure ($TcPO_2$) and prolonged time of 5X sit-to-stand test. The stratified comparison analysis indicated that severity of sarcopenia and DF ulcer, reduced $TcPO_2$, and grip strength were aggravated with the impaired foot-ankle function ($P < 0.05$). Multivariate Logistic analysis showed that age, $TcPO_2$, and severe sarcopenia were risk factors deteriorating the foot-ankle function.

Conclusion The sarcopenia is a key risk factor of decreasing foot-ankle function in patients with DF ulcer. Thus, the prevention of muscle mass and strength loss could be considered as part of comprehensive therapy for DF ulcer.

Keywords Diabetic foot ulcer, Sarcopenia, Foot and ankle function, Type 2 diabetic mellitus (T2DM)

Introduction

The diabetic foot (DF) ulcer is severe complication of type 2 diabetes mellitus (T2DM), which has become one of the main causes of disability and death. It is estimated that 9.1–26.1 million diabetic patients develop DF ulcers each year in worldwide [1], according to a national cohort study in Scotland, the overall incidence rate of DF ulcers was 11.2 per 1,000 person [2]. The therapy costs for DF ulcer become the financial burden.

In recent years, the incidence of T2DM in China has been rapidly increased. The prevalence of DF among T2DM patients is 25%, within which the rate of amputation is 26.4% [3]. It worsen the physical function and

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quality of life of T2DM patients. The foot and ankle joint play a vital role in maintaining proprioception, preserving balance and movement. Foot-ankle dysfunction can be characterized as gait changes, plantar pressure, pain, mobility and support stability. Factors including aging, reduced muscle strength, altered joint mobility, mechanical structural changes of foot, diabetic peripheral neuropathy (DPN) and diabetic peripheral vascular disease (DPVD) could affect foot-ankle function. These factors increase the risk of falls, bone fractures, and foot ulcers, leading to worse prognosis.

Sarcopenia is characterized as the loss of muscle mass and strength. Sarcopenia may affect physical mobility, resulting in the risk of fracture, disability, and even death [4, 5]. DF ulcer may worsen sarcopenia due to the infection and muscle dystrophy. Furthermore, patients with DF ulcer always showed long disease duration and muscle atrophy due to the long-term physical disability and restriction of movement. The combined effects of those factors result in changes of walking pattern and a decrease in overall body stability. It may increase the risk of developing ulcers, amputations and mortality. During the therapy of DF ulcer, the resistance to movement and bedridden lead to the quick muscle loss. The loss of muscle mass and strength forms a vicious circle and aggravates DF ulcer and impaired joint function in turn. However, the pathophysiology mechanism by which the reduced muscle mass and strength affect foot-ankle function was unclear. The sarcopenia may affect the foot-ankle function in DF ulcer patients, leading to prolonged recovery time and poor prognosis of physical function, thus compromise the quality of life. However, there were limited studies to clarify the relationship between sarcopenia and foot-ankle function in DF patients.

In this study, we aimed to clarify the effect of sarcopenia on foot-ankle function in patients with DF ulcer. It could provide clinical evidence for the early examination and prevention of muscle loss to achieve advanced foot-ankle function. The prevention and therapy for sarcopenia may be considered as part of comprehensive therapeutic strategy for DF ulcer.

Materials and methods

Study population

This study enrolled 108 patients with type 2 diabetic foot ulcer who were hospitalized in the Affiliated Hospital of Qingdao University from January 2021 to December 2022. Inclusion criteria: (1) meeting the diagnostic criteria of the Asian Working Group for Sarcopenia (AWGS) 2019 [6]; (2) age ranged from 18 to 80 years old, and diagnosed as T2DM according to the diagnostic standard of the World Health Organization (WHO) in 1999. All the Participants signed the informed consent. Exclusion criteria: (1) patients with type 1 DM (T1DM) or special types of DM; (2) patients with severe cardiac, liver and renal dysfunction, neurological diseases, bone and joint diseases, or autoimmune disorders; (3) bedridden for a long-term, or patients fitted with fracture internal fixation plates; (4) patients who are cognitively impaired and mentally ill; (5) malignant tumors, acute infectious diseases, or other chronic consumptive diseases.

General clinical data collection and laboratory tests

The general clinical data collection and test examinations were performed. We collected the general clinical characteristics including gender, age, body mass index (BMI is calculated as weight/height^2), duration of T2DM, and duration of DF ulcer. All patients were fasted for more than 12 h. The serum and plasma were collected and examined according to the standard protocol.

Assessment of Sarcopenia

Body composition was assessed by dual energy X-ray absorptiometry (DXA) (Norland, USA). Height-corrected appendicular skeletal muscle mass index [ASMI=limb skeletal muscle mass (kg)/height^2 (m^2)] was used. Based on the diagnostic consensus of AWGS 2019 [6], patient with the appendicular skeletal muscle mass index (ASMI) <7.0 kg/m^2 for men and <5.4 kg/m^2 for women is diagnosed with sarcopenia.

Muscle strength was assessed using a medical grip strength device. The patient was seated with their elbow bent at a 90° angle. The dominant hand was measured twice and the maximum value was recorded. According to the grip strength diagnostic thresholds of AWGS Consensus 2019 [6], the diagnostic criteria of sarcopenia is grip strength <28 kg for male, and <18 kg for female. The patient's trunk function was assessed using the 5X sit-to-stand test instead of using gait speed [6]. Patients were instructed to place their hands on their shoulders and stand up from a chair that was 46 cm in height. This process was recorded five times. The diagnostic criteria of reduced trunk function is that the patient takes 12 s or more to complete all 5 times of sit-stands. Based on AWGS Consensus of sarcopenia, patient with decreased muscle mass in their limbs, along with reduced muscle strength or trunk function is diagnosed as sarcopenia. In addition, if patient shows decreased muscle mass in their limbs along with reduced muscle strength and trunk function, they can be diagnosed with severe sarcopenia.

Grade assessment of diabetic foot ulcers

Grade assessment was conducted by medical professionals using the Wagner classification (Grade 0–5): Grade 0 represents a high-risk foot, with no ulceration but presenting risk factors for ulceration and infection; Grade 1 represents superficial ulceration without infection; Grade

2 indicates a moderately deep ulceration, often accompanied by soft tissue infection, without abscess or osteomyelitis; Grade 3 is characterized as deep ulceration, commonly accompanied by abscess and osteomyelitis; Grade 4 corresponds to localized gangrene, frequently associated with neuropathy, and Grade 5 denotes extensive or total foot gangrene [7].

Assessment of foot-ankle function and measurement of TcPO2

Specialists evaluate foot-ankle function using American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score [8]. According to the AOFAS ankle-hindfoot score, the ankle-foot function was evaluated and graded as "excellent, good, fair, poor" groups. The parameters included pain, function, autonomous activity, support, maximum walking distance, grand walking, abnormal gait, anteroposterior movement, hind-foot movement, ankle-hindfoot stability, and alignment. The grade was classified as Excellent group: 90 ~ 100 points, Good group: 75 ~ 89 points, Fair group: 50 ~ 74 points, and Poor group: <50 points (Suppl Table 1) [9]. The analysis of $TcPO_2$ was performed by skilled technicians using a TcPO2 analyzer manufactured (Radiometer Medical ApS, Denmark).

In order to minimize bias, two experienced physicians performed the AOFAS ankle-hindfoot scale assessments independently. Both physicians received comprehensive training on the administration and physical examination of the AOFAS ankle-hindfoot score from an experienced podiatrists.

Statistical analysis

The statistical analyses were conducted using SPSS Statistics 26.0. Results were presented as mean ± standard deviation (SD). The *t*-test was performed for comparison between two groups of normally distributed continuous data (mean ± SD). For comparison of continuous data among multiple groups, one-way analysis of variance (ANOVA) was used. For non-normally distributed continuous data, the comparison was conducted using non-parametric tests represented by median. Then we performed post-hoc analysis on these continuous data using Bonferroni correction. The comparison of categorical data was presented as percentages, and the analysis performed using the chi-squared test or Fisher's exact test. Logistic regression analysis was employed for the analysis of influencing factors. $P < 0.05$ was considered as statistically significant differences.

Table 1 Comparison of clinical characteristics between the Sarcopenia and non-sarcopenia groups in DF ulcer patients

	DF with sarcopenia (n = 44)	DF without sarcopenia (n = 64)	t/Z/χ^2 value	*P* value
Gender (male/female)	77.3%/22.7%	59.4%/40.6%	3.759	0.053
Age (years old)	67.27 ± 7.93	61.09 ± 9.43	3.565	0.001*
BMI (kg/m^2)	21.80 ± 2.45	24.57 ± 3.21	-4.83	< 0.001*
Duration of diabetes (years)	18.5 (10, 20)	10 (6, 19.5)	-2.972	0.003*
Duration of DF (days)	20.5 (14.25, 60)	15 (10, 41.25)	-1.154	0.249
Wagner classification (1/2/3/4/5)	13.6%/27.3%/29.5% 25%/4.5%	31.3%/43.8%/14.1% 10.9%/0	13.733	0.005*

Gender was assessed using the chi-squared test; Wagner classification was evaluated using Fisher's exact test; age and BMI were analyzed using the *t*-test, while the duration of diabetes and DF disease course were examined using non-parametric tests. *$P < 0.05$ indicates statistical significance. DF, diabetic foot; BMI, body mass index

Table 2 Comparison of indicators between the Sarcopenia and non-sarcopenia groups in DF patients

	DF with sarcopenia (n = 44)	DF without sarcopenia (n = 64)	Wald χ^2	*P* value
Lumbar T-score	-0.60 ± 1.37	0.08 ± 1.86	1.107	0.293
Femoral T-score	-1.33 ± 1.27	-0.77 ± 1.27	0.001	0.977
ASMI (kg/m^2)	6.40 (5.63, 6.78)	7.27 (6.56, 7.87)	61.796	< 0.001*
Grip strength (kg)	29 (23.7,30.78)	29.25 (22.73, 32.63)	9.987	0.002*
5X Sit-to-stand test (s)	15.28 (13.51, 17.97)	12.59 (10.67, 14.77)	5.129	0.024*
AOFAS ankle-hindfoot score	57 (45.5, 72)	76 (60.25, 87)	2.249	0.134
TcPO2 (mmHg)	16.65 (11, 25.7)	33.25 (17.08, 44.78)	8.775	0.003*

The generalized linear models (GLM) was used to examine the relationship between DF with or without sarcopenia and the key parameters. Age, sex, BMI, duration of diabetes, and Wagner classification were adjusted. *$P < 0.05$ indicates statistical significance

DF, diabetic foot; BMC, bone mineral content. ASMI, appendicular skeletal muscle mass index. 5X Sit-stand test, five-times sit-to-stand test. AOFAS, American Orthopaedic Foot and Ankle Society ankle-hindfoot score. $TcPO_2$, transcutaneous oxygenpressure

Results

Parameters of foot-ankle function aggravate in the DF patients with Sarcopenia

Patients with DF ulcer were divided into DF with sarcopenia group and DF without sarcopenia group. As shown in Tables 1 and 2, age, BMI, duration of diabetes, Wagner

classification, ASMI, Grip strength, 5X sit-to-stand test, transcutaneous oxygenpressure ($TcPO_2$), and serum creatine (sCr) were significant different between the two groups ($P<0.05$). DF with sarcopenia patients showed advanced age, lower BMI, longer duration of T2DM and DF ulcer, and more severe Wagner classification (Table 1). In addition, sarcopenia group showed reduced ASMI, grip strength, prolonged 5X sit-to-stand time, and reduced $TcPO_2$ (Table 2).

Comparison of clinical characteristics between DF patients with or without Sarcopenia

We compared the clinical characteristics between groups of DF with or without sarcopenia. In DF with sarcopenia group, patients showed higher sCr after adjusted age, sex, BMI, duration of DM, Wagner classification. There was no difference between two groups of the blood glucose level, including FBG and HbA1c, liver function, uric acid, UACR, or lipid profiles including total cholesterol (TC), triglyceride (TG), low-density-lipoprotein cholesterol (LDL-C) and high-density-lipoprotein cholesterol (HDL-C) (Table 3).

Table 3 Comparison of biochemical indicators between the Sarcopenia and non-sarcopenia groups in DF patients

	DF with sarcopenia (n = 44)	DF without sarcopenia (n = 64)	Wald χ^2	*P* value
HbA1c (%)	8.6 (7.7, 10.95)	8.3 (7.3, 9.45)	1.379	0.240
FBG (mmol/L)	5.23 (7.45, 8.92)	6.87 (5.49, 9.13)	1.134	0.287
ALB (g/L)	37.57 (32.75, 40.25)	39.17 (36.02, 41.95)	0.748	0.387
ALT (U/L)	16.5 (10.33, 22.53)	16.05 (12, 20.63)	0.510	0.475
AST (U/L)	15 (12.9, 19.73)	15.2 (12.93, 18.45)	0.621	0.431
TG (mmol/L)	0.99 (0.73, 1.45)	1.09 (0.83, 1.52)	0.052	0.820
TC (mmol/L)	4.48 ± 1.19	4.74 ± 1.20	0.802	0.370
HDL-C (mmol/L)	1.13 (0.94, 1.25)	1.07 (0.90, 1.32)	1.764	0.184
LDL-C (mmol/L)	2.70 ± 1.06	2.99 ± 0.99	0.752	0.386
sCr (umol/L)	77.35 (56.75, 101.8)	64.6 (52.25, 87.73)	3.904	0.048*
UA (umol/L)	324.05 ± 107.56	313.28 ± 79.40	0.483	0.487
UACR (mg/g)	243.26 (28.33, 1045.85)	45.69 (15.45, 236.71)	0.220	0.639
WBC (*10^9/L)	9 (6.11, 11.73)	7.53 (6.29, 9.54)	0.204	0.652
CRP (mg/L)	20.21 (9.37, 53.46)	10.07 (1.94, 17.09)	1.452	0.228

The generalized linear models (GLM) was used to analyzed the relationship between DF with or without sarcopenia and the key parameters. Age, sex, BMI, duration of diabetes, and Wagner classification were adjusted. *$P<0.05$ indicates statistical significance

DF, diabetic foot; HbA1c, Hemoglobin A1c; FBG, fasting blood glucose; ALB, Albumin; ALT, Alanine transaminase; AST, Aspartate transaminase; TG, triglyceride; TC, total cholesterol; LDL-C, low-density-lipoprotein cholesterol; HDL-C, high-density-lipoprotein cholesterol; sCr, serum creatine; UA, uric acid; UACR, Urinary albumin creatinine ratio; WBC, white blood cell; CRP, C-reactive protein

The stratified comparison analysis of foot-ankle function in patients with DF ulcer

The ankle-foot function was evaluated and graded as "excellent, good, fair, poor" groups according to the AOFAS ankle-hindfoot score [8] (Suppl Table 1). The univariate analysis showed that age, severity of ulcer, sarcopenia severity, $TcPO_2$, grip strength, 5X sit-to-stand test, lumbar T-score, femoral T-score were significant different among excellent, good, fair and poor groups of foot-ankle function in patients with DF ulcer ($P<0.05$) (Table 4). The foot-ankle function significantly exacerbated with aging. The severity of ulcer and sarcopenia, including grip strength, 5X sit-to-stand test, and $TcPO_2$ deteriorated with the progression of impaired foot-ankle function. In addition, TG, HDL-C, D-dimer, and CRP were significantly different among excellent, good, fair and poor groups of foot-ankle function ($P<0.05$) (Table 4). The stratified comparison analysis indicated that severity of sarcopenia and DF ulcer, grip strength, 5X sit-to-stand test, reduced $TcPO_2$, and bone mineral density (BMD) were aggravated with the impaired foot-ankle function.

Logistic analysis of the factors influencing foot-ankle function in DF ulcer patients

Multivariate Logistic regression analysis showed that the age, $TcPO_2$, and severity of sarcopenia were independent risk factors for foot-ankle function. Compared to patients with severe sarcopenia, the odds ratio (OR) was 0.056 ($P=0.032$), 0.082 ($P=0.041$), and 0.091 ($P=0.043$) in sarcopenia grading of 0, 1, and 2 patients, respectively (Table 5). The $TcPO_2$, age, and sarcopenia severity were identified as the vital risk factors influencing foot-ankle function in DF ulcer patients.

Discussion

In this study, we investigated the relationship of sarcopenia and foot-ankle function in patients with DF ulcer. Sarcopenia was identified as the risk factor which affecting foot-ankle function. The AOFAS ankle-hindfoot scores were significantly reduced in sarcopenia group compared to those of non-sarcopenia. Furthermore, the stratified comparison of foot-ankle function showed that the impaired foot-ankle function deteriorated with the severity of sarcopenia. Thus, our study provided clinical evidence that sarcopenia aggravates the foot-ankle function in DF ulcer. The early examination and intervention of sarcopenia should be considered to defense the muscle wasting during the long-term comprehensive therapy for DF ulcer.

It is widely recognized that skeletal muscles play a crucial role in providing support and protection to joints. Impaired skeletal muscle function could lead to the decreased mobility and increased risk of falls and bone

Table 4 Stratified comparison of foot-ankle function in patients with type 2 diabetic foot

	Excellent group (n = 12)	Good group (n = 30)	Fair group (n = 40)	Poor group (n = 26)	*P* value
Clinical characteristics					
Age (year)	52 (47.25, 59.25)	59.5 (57.75, 65)	66.5(58.5, 71.75) [a, b]	72 (69, 76.25) [a, b, c]	< 0.001*
BMI (kg/m2)	23.94 ± 3.32	23.93 ± 2.84	23.63 ± 3.54	22.36 ± 2.96	0.257
Duration of DM (year)	11 (9.25, 17.75)	9 (4.75, 18.5)	15 (7.5, 20)	16.5 (10, 20)	0.056
Duration of DF (year)	10 (7, 60)	15 (10, 30)	20 (10, 30)	30 (15, 60)	0.052
Parameters of sarcopenia and foot-ankle function					
Ulceration severity (mild/moderate/severe)	25%/75%/0	33.3%/63.3%/3.3%	25%/62.5%/12.5%	11.55%/34.6%/53.8% [a, b, c]	< 0.001*
Sarcopenia classification (None/Reduced muscle mass/ Sarcopenia/Severe sarcopenia)	83.3%/16.7%/0/0	70%/3.3%/26.7%/0	42.5%/7.5%/47.5%/2.5% [a]	34.6%/3.8%/19.2%/42.3% [a, b]	< 0.001*
Grip strength	33.25 (25.53, 34.2)	32.4 (29.63, 34.13)	29.1 (22.83, 31.1)[b]	23.45 (17.05, 28.73) [a, b]	< 0.001*
5X sit-to-stand test	11.20 (9.93, 13.06)	13.10 (11.04, 14.47)	13.39 (12.69, 16.93) [a]	17.81 (13.86, 19.52) [a, b, c]	< 0.001*
TcPO2	44.55 (42.68, 48.65)	36.9 (26.38, 45.7)	22 (13.13, 29.6) [a, b]	11.7 (10.45, 16.25) [a, b, c]	< 0.001*
Lumbar T score	1.71 (0.78, 2.58)	0.2 (-1.07, 0.80) [a]	-0.15 (-1.43, 0.74) [a]	-1.5 (-2.23, -0.70) [a, b]	< 0.001*
Femoral T score	0.18 ± 1.17	-0.90 ± 1.12	-1.07 ± 1.26 [a]	-1.56 ± 1.27 [a]	0.001*
Biochemical data					
HbA1c (%)	9.15 (7.73, 10.95)	8.55 (7.35, 10.5)	8.5 (7.22, 9.65)	8.3 (7.22, 9.75)	0.59
FBG (mmol/L)	8.69 (7.55, 9.93)	6.38 (5.75, 8.35)	7.63 (5.26, 8.95)	6.42 (5.14, 8.38)	0.25
C-P (nmol/L)	0.93 (0.61, 1.70)	1.44 (0.93, 1.91)	1.24 (0.63, 1.80)	1.64 (0.95, 2.26)	0.228
FINS (mIU/L)	5.96 (1.47, 11.92)	5.99 (2.30, 8.85)	4.19 (1.65, 8.31)	5.68 (2.15, 14.72)	0.604
ALB (g/dL)	36.3 (30.95, 41.75)	38.99 (35.28, 41.43)	37.79 (32.37, 42)	39.33 (34.60, 41.1)	0.704
ALT (U/L)	16.25 (11.58, 21.75)	15 (12, 18.63)	17.5 (12, 23.25)	16 (10.75, 24.48)	0.6
AST (U/L)	15.55 (12.1, 18.9)	14.15 (11.95, 18)	16 (13.6, 18.98)	15 (13, 21.70)	0.409
TG (mmol/L)	1.62 (1.40, 2.22)	1 (0.83, 1.42) [a]	1.01 (0.74, 1.53)	1.03 (0.82, 1.33)	0.04*
TC (mmol/L)	5.01 ± 0.98	4.27 ± 0.91	4.67 ± 1.23	4.63 ± 1.20	0.113
HDL-C (mmol/L)	0.96 ± 0.24	1.02 ± 0.25	1.21 ± 0.33	1.17 ± 0.33	0.017*
LDL-C (mmol/L)	3.31 (2.48, 4.44)	2.64 (2.16, 3.14)	2.95 (2.1, 3.37)	2.78 (1.99, 3.76)	0.24
BUN (mmol/L)	6.51 (4.83, 8.19)	6.14 (5.13, 7.21)	6.34 (5.24, 7.76)	7.14 (6.01, 8.58)	0.246
sCr (umol/L)	76.4 (46.48, 95.05)	70.15 (52.25, 89.45)	65.05 (52.25, 87.38)	64.7 (58.5, 95.58)	0.867
UA (umol/L)	336.55 (304.5, 389.9)	293.3 (243.25, 327.83)	300.5 (244.75, 367.1)	338.8 (263.68, 415.83)	0.14
UACR (mg/gCr)	40.15 (11.18, 885.58)	51.59 (14.8, 324.85)	48.43 (16.83, 636.59)	347 (42.65, 820.52)	0.142
D-dimer	335 (172.5, 377.5)	345 (197.5, 392.5)	375 (322.5, 455)	390 (357.5, 460)	0.028*
WBC (*10^9/L)	8.11 (6.68, 9.75)	7.31 (6.27, 9.42)	8.21 (5.66, 11.3)	7.79 (6.23, 11.15)	0.937
CRP (mg/dL)	11.38 (5.19, 19.72)	7.78 (0.88, 16.22)	11.05 (3.46, 35.44)	16.4 (10.32, 43.3) [b]	0.028*

BMI, femoral T-score, TC, and HDL-C were analyzed using the F-test. The remaining indicators were assessed using the Kruskal-Wallis rank test. We used the Bonferroni correction for post-hoc analysis. *$P < 0.05$ indicates statistical significance. [a] indicates that compared with the Excellent group, $P < 0.05$; [b] indicates that compared with the Good group, $P < 0.05$; [c] indicates that compared with the Fair group, $P < 0.05$; both pairwise comparisons have undergone multiple corrections

According to the diagnostic criteria of AWGS 2019, the severity of sarcopenia can be classified as: no sarcopenia, reduced muscle mass, sarcopenia, and severe sarcopenia

According to the AOFAS ankle-hindfoot score, the ankle-foot function was evaluated and graded as "excellent, good, fair, poor" groups. The grade was classified as Excellent group: 90 ~ 100 points, Good group: 75 ~ 89 points, Fair group: 50 ~ 74 points, and Poor group: <50 points (Suppl Table 1)

DF, diabetic foot; TcPO2, transcutaneous oxygenpressure; HbA1c, Hemoglobin A1c; FBG, fasting blood glucose; C-P, C-peptide; FINS, fasting insulin; ALB, Albumin; ALT, Alanine transaminase; AST, Aspartate transaminase; TG, triglyceride; TC, total cholesterol; LDL-C, low-density-lipoprotein cholesterol; HDL-C, high-density-lipoprotein cholesterol; BUN, Blood urea nitrogen; sCr, serum creatine; UA, uric acid; UACR, Urinary albumin creatinine ratio; WBC, white blood cell; CRP, C-reactive protein

fractures. Recent studies indicate that the prevalence of sarcopenia among elderly Chinese patients with diabetes is 14.8% [10]. However, studies on sarcopenia in the DF population are limited. Previous studies indicated that sarcopenia in DF patients was associated with advanced age, longer duration of diabetes, poor glycemic control, and impaired vascular function [11, 12]. Oxidative stress and inflammation infiltration may disrupt the balance between muscle synthesis and degradation, thereby exacerbating muscle atrophy [13]. Severe lower extremity stenosis and DPN in DF patients, combined with factors including infections, malnutrition, immobility, could

Table 5 Multivariate logistic regression analysis of factors influencing foot-ankle function in patients with DF

	B	SE	Wald	P	OR (95%CI)
foot-ankle function = 1	-5.086	2.828	3.233	0.072	0.006 (0.000, 1.580)
foot-ankle function = 2	-2.437	2.810	0.752	0.386	0.087 (0.000, 21.556)
foot-ankle function = 3	0.578	2.812	0.042	0.837	1.782 (0.007, 441.110)
Age	0.082	0.034	5.880	0.015*	1.085 (1.016, 1.159)
Sex (versus female)	-0.799	0.459	3.035	0.081	0.450 (0.183, 1.105)
BMI (kg/m2)	-0.022	0.070	0.094	0.760	0.979 (0.853, 1.124)
Duration of DM (years)	-0.034	0.028	1.503	0.220	0.967 (0.916, 1.020
TcPO2	-0.077	0.025	9.683	0.002*	0.926 (0.883, 0.972)
CRP	0.003	0.009	0.116	0.733	1.003 (0.986, 1.020)
Severity of Foot Ulcer = 1	-0.969	0.788	1.510	0.219	0.380 (0.081, 1.780)
Severity of Foot Ulcer = 2	-1.113	0.696	2.562	0.109	0.328 (0.084, 1.284)
Severity of Foot Ulcer = 3	reference				
Sarcopenia Grading = 0	-2.884	1.342	4.591	0.032*	0.056 (-5.592, -0.252)
Sarcopenia Grading = 1	-2.495	1.222	4.168	0.041*	0.082 (-5.024, -0.161)
Sarcopenia Grading = 2	-2.393	1.182	4.098	0.043*	0.091 (0.009, 0.927)
Sarcopenia Grading = 3	reference				

B: Partial Regression Coefficient; SE: Standard Error; OR: Odds Ratio; 95% CI: 95% Confidence Interval; $TcPO_2$, transcutaneous oxygenpressure; CRP, C-reactive protein

We used ordinal logistic regression analysis, and adjusted for age, sex, BMI, duration of diabetes, TcPO2, CRP, severity of foot ulcer, and sarcopenia grading in the model. *$P<0.05$ indicates statistical significance

The assignment of foot-ankle function is as follows: Excellent foot-ankle function group is assigned a value of 1, Good group is assigned a value of 2, Fair group is assigned a value of 3, and Poor foot-ankle function group is assigned a value of 4. The assessment of severity of foot ulcer is as follow: Mild degree of foot ulceration is assigned as value of 1, Moderate is assigned as value of 2, Severe is assigned as value of 3. Evaluation of sarcopenia severity is assigned as follows: No sarcopenia is assigned a value of 0, Reduced muscle mass is assigned a value of 1, Sarcopenia is assigned a value of 2, and Severe sarcopenia is assigned a value of 3

potentially increase the risk of sarcopenia and deteriorate the progression. DPN leads to the loss of motor units and reduction in nerve fibers, resulting in atrophy of lower extremity muscles and reduced muscle strength, especially in the intrinsic muscles of the lower extremities [14, 15]. With the neuro-degeneration, the skeletal muscle atrophy was progressive, leading to the alterations in the structure, gait, and changes in foot pressure. Those factors contribute to the increased risk of foot ulcers. Diabetic autonomic neuropathy leads to abnormal sweat secretion, dry and cracked skin, facilitating the formation of calluses, and alters foot pressure. Moreover, the opening of arteriovenous shunts is increased, results in the lower extremity hemodynamic disorders [16, 17]. The sensory abnormalities caused by DPN could manifest as lost of pain, temperature, and touch sensations. This lack of protective sensation leads to the exacerbating the occurrence of DF [18]. DPN impacts the sensory, motor, and autonomic nervous systems. It can also result in bone deformities, restricted joint mobility, unstable gait, and increased plantar pressure. In the condition of trauma, it can further lead to the development of DF ulcer [18–20]. Multiple studies have indicated that alterations in gait and body stability in T2DM patients occur before the clinical symptoms of DPN [21–23].

$TcPO_2$ is a vital factor affecting foot-ankle function. DPVD results in heightened plantar pressure in T2DM patients. The increased pressure leads to the compression of plantar capillaries, and microangiopathy, then results in a vicious cycle [25]. Jung et al. reported that muscle mass in DF patients was related to the lower limb preservation [26]. In addition, sarcopenia increases the risk of mortality in diabetic amputees. The lower skeletal muscle capillarization may affect exercise capacity with aging [27]. A cross-sectional study suggested that decreased capillary density in skeletal muscles was observed in elderly individuals with sarcopenia, and the severity of sarcopenia was correlated with skeletal muscle capillarization [29]. Atherosclerosis occurs in T2DM patients due to poor glycemic control and dyslipidemia, leading to lower extremity arterial occlusion. The primary manifestations include intermittent claudication, rest pain, ulcers, and gangrene, which can affect the patient's gait and balance stability [29]. A few studies reveal that peripheral arterial disease (PAD) is an independent risk factor for amputation in patients with DF [30–32].

There are several limitations of this study. First, this study was a cross-sectional observational study. We did not conduct the analysis of fellow-up and prognosis due to the poor compliance of DF patients. Further investigation associated with prognosis and long-term fellow-up will be performed in the future. Second, this study was conducted in small sample size. We will expand the sample size to provide firm clinical evidence. Third, several factors associated with sarcopenia were not included in this study, such as detailed evaluation of nutrition condition, exercise restriction, bedrest duration, anti-diabetic agents.

In summary, we indicated that DF patients with sarcopenia showed deteriorated foot-ankle function compared to those without sarcopenia. The severity of sarcopenia, age, and $TcPO_2$ are the risk factors for impaired foot-ankle function in DF patients. Therefore, it is necessary to recognize the impact of sarcopenia on foot-ankle

function, to improve quality of life, and decrease the risk of falls, fractures, and even mortality in aged T2DM patients.

Conclusion

In conclusion, the sarcopenia aggravates the foot-ankle function in patients with DF ulcer. Thus, the prevention of muscle mass and strength loss could be considered as part of comprehensive therapy for DF ulcer to improve the prognosis.

Abbreviations

T2DM	type 2 diabetic mellitus
T1DM	type 1 diabetic mellitus
DF	diabetic foot
DXA	dual energy X-ray absorptiometry
AOFAS	American Orthopaedic Foot and Ankle Society
BMI	Body mass index
ASMI	appendicular skeletal muscle mass index
$TcPO_2$	transcutaneous oxygenpressure
AWGS	Asian Working Group for Sarcopenia
FINS	fasting insulin
UACR	urinary albumin creatinine ratio
CRP	C-reactive protein
BMD	bone mineral density
BMC	bone mineral content
DPN	diabetic peripheral neuropathy
DPVD	diabetic peripheral vascular disease
OR	odds ratio
SD	standard deviation
ANOVA	analysis of variance
HbA1c	Hemoglobin A1c
FBG	fasting blood glucose
C-P	C-peptide
ALT	Alanine transaminase
AST	Aspartate transaminase
TG	triglyceride
TC	total cholestero
LDL-C	low-density-lipoprotein cholesterol
HDL-C	high-density-lipoprotein cholesterol
BUN	Blood urea nitrogen
WBC	white blood cell

Supplementary Information

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Supplementary Material 1

Author contributions

Weina Kuang collected the clinical data, and Shujing An performed statistical analysis. Shujing An, Weina Kuang and DBZ wrote the manuscript. Yonglu Hu and Xinwei Li assisted the study. Yangang Wang provided helpful suggestion. Chengqian Li and Bingzi Dong conceived and designed the study. Chengqian Li supervised project. Shujing An and Weina Kuang contributed equally to this work.

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Data availability

The data generated and analyzed is included in the publication. Further detailed data are available from the corresponding author on reasonable request.

Declarations

Ethical approval

This study was approved by the ethics committee of the Affiliated Hospital of Qingdao University. All procedures performed in this study involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The written informed consent from all the participants was obtained.

Disclosure Statement

All authors have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to the publication.

Competing interests

The authors declare no competing interests.

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References

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and their recurrence. N Engl J Med. 2017;376:2367–75.
2. Chamberlain RC, Fleetwood K, Wild SH, Colhoun HM, Lindsay RS, Petrie JR, McCrimmon RJ, Gibb F, Philip S, Sattar N, Kennon B, Leese GP. Foot Ulcer and Risk of Lower Limb amputation or death in people with diabetes: a National Population-based Retrospective Cohort Study. Diabetes Care. 2022;45:83–91.
3. Y.L.M.S.P.L.Z.D Q, Li C. Status and Future Development Direction of Plantar Offloading Treatment for Diabetic Foot patients in China. Clin Rev. 2018;33:97–9.
4. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48:601.
5. Petermann-Rocha F, Balntzi V, Gray SR, Lara J, Ho FK, Pell JP, Celis-Morales C. Global prevalence of Sarcopenia and severe Sarcopenia: a systematic review and meta-analysis. J cachexia Sarcopenia Muscle. 2022;13:86–99.
6. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, Jang HC, Kang L, Kim M, Kim S, Kojima T, Kuzuya M, Lee JSW, Lee SY, Lee WJ, Lee Y, Liang CK, Lim JY, Lim WS, Peng LN, Sugimoto K, Tanaka T, Won CW, Yamada M, Zhang T, Akishita M, Arai H. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia diagnosis and treatment. J Am Med Dir Assoc. 2020;21:300–e307302.
7. Wagner FW Jr. The dysvascular foot: a system for diagnosis and treatment. Foot Ankle. 1981;2:64–122.
8. Van Lieshout EM, De Boer AS, Meuffels DE, Den Hoed PT, Van der Vlies CH, Tuinebreijer WE, Verhofstad MH. American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score: a study protocol for the translation and validation of the Dutch language version. BMJ open. 2017;7:e012884.
9. Pinsker E, Daniels TR. AOFAS position statement regarding the future of the AOFAS Clinical Rating systems. Foot Ankle Int. 2011;32:841–2.
10. Sanz-Cánovas J, López-Sampalo A, Cobos-Palacios L, Ricci M, Hernández-Negrín H, Mancebo-Sevilla JJ, Álvarez-Recio E, López-Carmona MD, Pérez-Belmonte LM, Gómez-Huelgas R. M.R. Bernal-López, Management of type 2 diabetes Mellitus in Elderly patients with Frailty and/or Sarcopenia. Int J Environ Res Public Health, 19 (2022).
11. Yang Q, Ni X, Zhang Y, Zhu B, Zeng Q, Yang C, Shi J, Zhang C, Cai J, Hu J, Li Q, Jiang Y, Cheng Q, Cheng C. Sarcopenia is an independent risk factor for all-cause mortality rate in patients with diabetic foot ulcers. Front Nutr. 2023;10:1097008.
12. Xu X, Li C, Diao H, Guo Y, Zhao Y, Zhao W, Dong B. Elevated circulating follicle stimulating hormone level is associated with dyslipidemia in male type 2 diabetes mellitus patients: a cross-sectional study. Diab/Metab Res Rev. 2024;40:e3718.

13. Zheng J, Hasting MK, Zhang X, Coggan A, An H, Snozek D, Curci J, Mueller MJ. A pilot study of regional perfusion and oxygenation in calf muscles of individuals with diabetes with a noninvasive measure. J Vasc Surg. 2014;59:419–26.
14. Marshall A, Alam U, Themistocleous A, Calcutt N, Marshall A. Novel and emerging electrophysiological biomarkers of Diabetic Neuropathy and painful Diabetic Neuropathy. Clin Ther. 2021;43:1441–56.
15. Andersen H, Gjerstad MD, Jakobsen J. Atrophy of foot muscles: a measure of diabetic neuropathy. Diabetes Care. 2004;27:2382–5.
16. Pasnoor M, Dimachkie MM, Kluding P, Barohn RJ. Diabetic neuropathy part 1: overview and symmetric phenotypes. Neurol Clin. 2013;31:425–45.
17. Dong B, Lv R, Wang J, Che L, Wang Z, Huai Z, Wang Y, Xu L. The Extraglycemic Effect of SGLT-2is on Mineral and Bone metabolism and bone fracture. Front Endocrinol. 2022;13:918350.
18. Boucher P, Teasdale N, Courtemanche R, Bard C, Fleury M. Postural stability in diabetic polyneuropathy. Diabetes Care. 1995;18:638–45.
19. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293:217–28.
20. Fernando DJ, Masson EA, Veves A, Boulton AJ. Relationship of limited joint mobility to abnormal foot pressures and diabetic foot ulceration. Diabetes Care. 1991;14:8–11.
21. Fernando M, Crowther R, Lazzarini P, Sangla K, Cunningham M, Buttner P, Golledge J. Biomechanical characteristics of peripheral diabetic neuropathy: a systematic review and meta-analysis of findings from the gait cycle, muscle activity and dynamic barefoot plantar pressure, clinical biomechanics (Bristol. Avon). 2013;28:831–45.
22. Sawacha Z, Gabriella G, Cristoferi G, Guiotto A, Avogaro A, Cobelli C. Diabetic gait and posture abnormalities: a biomechanical investigation through three dimensional gait analysis. Clin Biomech (Bristol Avon). 2009;24:722–8.
23. Vaz MM, Costa GC, Reis JG, Junior WM, Albuquerque de Paula FJ, Abreu DC. Postural control and functional strength in patients with type 2 diabetes mellitus with and without peripheral neuropathy. Arch Phys Med Rehabil. 2013;94:2465–70.
24. Morrison S, Colberg SR, Parson HK, Vinik AI. Relation between risk of falling and postural sway complexity in diabetes. Gait Posture. 2012;35:662–8.
25. Pataky Z, Golay A, Bounameaux H, Bobbioni-Harsch E, Assal JP. Relationship between peripheral vascular disease and high plantar pressures in diabetic neuro-ischaemic patients. Diabetes Metab. 2003;29:489–95.
26. Jung SY, Lee MJ, Lee SY. Analysis of the Relationship between Lower leg muscle Mass and Preservation of Lower Extremity in patients with Diabetic Foot Ulcer, the international journal of lower extremity wounds, 22 (2023) 503–8.
27. Kim YK, Lee HS, Ryu JJ, Lee HI, Seo SG. Sarcopenia increases the risk for mortality in patients who undergo amputation for diabetic foot. J Foot Ankle Res. 2018;11:32.
28. Prior SJ, Ryan AS, Blumenthal JB, Watson JM, Katzel LI, Goldberg AP. Sarcopenia is Associated with lower skeletal muscle capillarization and Exercise Capacity in older adults. J Gerontol A. 2016;71:1096–101.
29. McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, Chan C, Celic L, Pearce WH, Schneider JR, Sharma L, Clark E, Gibson D, Martin GJ. Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. JAMA. 2001;286:1599–606.
30. Jeyaraman K, Berhane T, Hamilton M, Chandra AP, Falhammar H. Amputations in patients with diabetic foot ulcer: a retrospective study from a single centre in the Northern Territory of Australia. ANZ J Surg. 2019;89:874–9.
31. Ting Xiao AW, Xu Z, Wang Y, Jiang Y, Gu H, Ji Q. Ying Lan, analysis of factors related to Diabetic Foot Amputation in 436 cases. Chin J Endocrinol Metabolism. 2009;06:591–4.
32. Dai W, Li Y, Huang Z, Lin C, Zhang XX, Xia W. Predictive factors and nomogram to evaluate the risk of below-ankle re-amputation in patients with diabetic foot. Curr Med Res Opin. 2022;38:1823–9.

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