



# Clinical Characteristics, Treatment, and Prognosis of Diabetic Foot Disease in Macao and Beijing: A Retrospective Study

Yang Zhang · Nim Choi · Gangzhu Liang · Tan Li · Chun-man Ieong ·  
Sio-in Chu · Chengjie Wang · Qi Wang · Hui Li

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## ABSTRACT

**Introduction:** There has been no epidemiological study of diabetes mellitus (DM) in Macao. Also, multidisciplinary treatment is yet to be popularized and complications of DM cannot be managed promptly in this region. Therefore, this study was performed to compare the clinical characteristics, treatment, and prognosis of

diabetic foot disease between patients in Macao and Beijing.

**Methods:** A total of 243 patients with diabetic foot disease were enrolled: 124 from a tertiary hospital in Beijing and 119 from a tertiary hospital in Macao. The clinical profiles were collected and analyzed.

**Results:** The surgical treatment rate in the Beijing group (96.0%) was significantly higher than that in the Macao group (21.0%) ( $P < 0.05$ ). The overall mortality rate was 14.8%, and cardiac failure was the most common cause (72.2%). Monthly household income and smoking were independent factors affecting the age of onset. Age of diabetes onset was a risk factor for the occurrence of diabetic foot disease; age, duration of diabetic foot disease, and length of smoking history were independent factors affecting the severity of diabetic foot disease. Renal dysfunction and activated partial thromboplastin time were independent factors affecting the survival time of patients with diabetic foot disease.

**Conclusions:** Smoking may be a risk factor for the occurrence and development of diabetic foot; it can significantly reduce the onset age and aggravate the severity of this disease. The onset age of diabetic foot was lower in high-income patients, and prevention should be encouraged in this population. Elderly age may be associated with a rapidly developing and severe diabetic foot. The clinical course was also associated with the severity of diabetic foot.

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Y. Zhang · T. Li · C. Wang · Q. Wang  
Department of Vascular Surgery, Beijing Chaoyang  
Hospital, Capital Medical University, Beijing  
100020, China

N. Choi · G. Liang  
Department of General Surgery, Hospital Conde S.  
Januário, Macau 999078, China

C. Ieong · S. Chu  
Department of Radiology, Hospital Conde S.  
Januário, Macau 999078, China

H. Li (✉)  
Department of Thoracic Surgery, Beijing Chaoyang  
Hospital, Capital Medical University, Beijing  
100020, China  
e-mail: huilee@vip.sina.com

Renal and coagulation function should be closely monitored during the treatment of diabetic foot.

**Keywords:** Beijing; Diabetic foot; Macao; Risk factor

### Key Summary Points

There has been no epidemiological study of DM in Macao. Also, multidisciplinary treatment is yet to be popularized and complications of DM cannot be managed promptly in this region.

This study was performed to compare the clinical characteristics, treatment, and prognosis of diabetic foot disease between patients in Macao and Beijing.

Smoking was a risk factor for the occurrence and development of diabetic foot; it significantly reduced the onset age and aggravated the severity of this disease.

Age of diabetic foot onset was lower in high-income patients, and prevention should be encouraged in this population.

Renal and coagulation function should be closely monitored during the treatment of diabetic foot.

## INTRODUCTION

Diabetes mellitus (DM) is one of the most common metabolic diseases globally, and the prevalence of DM has been increasing in the last few decades [1]. It is expected to affect 592 million individuals by 2035, resulting in a severe and growing global health burden [2]. Diabetic foot disease is a major complication of DM that can lead to the amputation of the lower limbs and is the leading cause of death in patients with DM. Diabetic foot ulceration (DFU) is skin damage with a loss of epithelial tissue on the foot; it can involve the corium,

muscles, and even bone. DFU has high morbidity and mortality [3]. Histopathologically, DFU is characterized by ischemia, neuropathy, and infection [4]. Additionally, approximately 35% of all patients with DFU have concomitant peripheral arterial disease (PAD) [5]. PAD is usually clinically underdiagnosed, as less than 25% of all PAD cases experience notable symptoms such as intermittent claudication and rest pain [6]; nevertheless, it has been identified as an independent risk factor for DFU and amputation [7]. PAD reduces the blood supply to the lower extremities, which may aggravate the foot infection, delay wound healing, and even lead to gangrene. Therefore, early diagnosis and management of DFU and PAD are crucial in order to improve the clinical prognosis of diabetic foot disease [3].

DM is the fifth leading cause of death in Macao. The incidence of DM in the general population of Macao is 8.6%, and an increasing number of young adults are affected. DM severely impairs the social labor force and the average life expectancy in this region. There is no epidemiological study of DM in Macao. Also, multidisciplinary treatment is still uncommon and complications of DM are not managed promptly. Therefore, in the current study, we compared the clinical characteristics, treatment, and prognosis of diabetic foot disease between patients in Macao and Beijing.

## METHODS

### Subjects

This study enrolled a total of 243 patients with diabetic foot disease between January 2013 and December 2018, including 124 patients from a tertiary hospital in Beijing (the Beijing group) and 119 patients from a tertiary hospital in Macao (the Macao group). This study was approved by the local ethics committee. Written informed consent was obtained from each participant. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Patients who were diagnosed with diabetic foot through medical history collection, clinical

examination, imaging examination, and laboratory examination were included. Patients who missed multiple clinical examinations and those for whom there were substantial missing data were excluded. Patients with severe mental illness or a disturbed consciousness who could not complete the investigations as required were excluded.

Among the 243 patients, 232 were Han (95.5%) and 11 were other ethnicities (4.5%). In the Beijing group, 120 patients were Han (96.8%) and 4 (3.2%) were other ethnicities. In the Macao group, 112 patients were Han (94.1%) and 7 (5.9%) were other ethnicities. There was no significant difference in the distribution of ethnic groups between the two groups according to the results of a chi-square test ( $\chi^2 = 0.992$ ,  $P = 0.319$ ).

## Diagnosis

Diagnosing diabetic foot early is difficult. Patients usually consult a doctor when they develop clinical symptoms such as foot infection, decreased or lost sensation, foot deformities, and intermittent claudication of the lower limbs. Foot ulcer is the most common clinical manifestation of diabetic foot, with neuropathy, vascular disease, and infection as the main causes.

The current view is that ulcers can cause infection rather than being caused by infection. Therefore, we consider DM patients with infected wounds of the foot that have not healed after 14 days to have diabetic foot disease, and these patients require further relevant examination.

The ankle-brachial index (ABI) test is the main test for diabetic vascular disease. Neuropathy is usually diagnosed based on clinical manifestations and the diagnosis is corroborated by neuroelectrophysiology. A 10g nylon wire is applied to four different parts of the foot to check for loss of sensation, and diabetic foot is diagnosed based on positive results from any of the following tests: the 128 Hz tuning fork test; vibration acupuncture; the ankle reflex test; and the vibration perception threshold.

## Data Collection

The clinical profiles and follow-up data were collected and analyzed. General characteristics included age, sex, marital status, occupation, and income. Clinical variables included smoking history, hypertension, hyperlipidemia, coronary heart disease, stroke, renal dysfunction, peripheral neuropathy, retinopathy, history of stent implantation, and the progression time of diabetic foot disease (i.e., the time from the diagnosis of DM to the diagnosis of diabetic foot disease). Laboratory parameters included serum alanine transaminase level (ALT), serum aspartate aminotransferase level (AST), serum triglyceride level (TG), serum total cholesterol level (TC), serum low-density lipoprotein cholesterol level (LDL-C), serum high-density lipoprotein cholesterol level (HDL-C), red blood cell count (RBC), platelet count (PLT), creatinine level (Cr), blood urea nitrogen level (BUN), hemoglobin level (HGB), activated partial thromboplastin time (APTT), blood glucose level, and urine protein. Cardiac function parameters included left ventricular interior diameter (LVID), left ventricular end-diastolic diameter (LVEDD), and left ventricular function (LVEF).

## Statistical Analysis

SPSS 24.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analyses. All analyses were two-sided, and the statistical significance level was set at 0.05. Continuous variables were expressed as the mean  $\pm$  standard deviation (SD) when normally distributed or the median (interquartile range, IQR) when non-normally distributed. Categorical variables were presented as frequencies (percentage, %). Univariate statistical analysis utilized the independent-sample *t* test, analysis of variance (ANOVA), chi-square test, or rank-sum test, as appropriate. To identify the potential risk factors for DM, multivariate logistic regression analyses, multiple linear regression analyses, and Kaplan–Meier survival analyses were used.

**Table 1** Characteristics of patients with DM

Variable	Beijing group ( <i>n</i> = 124)	Macao group ( <i>n</i> = 119)	$\chi^2/Z$ value	<i>P</i> value
Sex				
Male	85 (68.5%)	65 (54.6%)	4.985	0.026
Female	39 (31.5%)	54 (45.4%)		
Marital status				
Single/divorced/widowed	54 (43.5%)	17 (14.3%)	25.143	< 0.001
Married/cohabiting	70 (56.5%)	102 (85.7%)		
Smoking history				
Never smoking	66 (53.2%)	71 (59.6%)	3.983	0.136
Already quit smoking	7 (5.6%)	12 (10.1%)		
Current smoking	51 (41.2%)	36 (30.3%)		
Number of cigarettes smoked				
0 cigarettes	66 (56.4%)	71 (66.4%)	− 1.341	0.180
1–20 cigarettes	33 (28.2%)	21 (19.6%)		
≥ 21 cigarettes	18 (15.4%)	15 (14.0%)		
Length of smoking history				
0 year	66 (56.4%)	71 (66.4%)	− 2.582	0.010
1–30 years	11 (9.4%)	26 (24.3%)		
≥ 31 years	40 (34.2%)	10 (9.3%)		

## RESULTS

In the Beijing group, there were 85 males and 39 females with an average age of  $70.86 \pm 9.60$  years; 54 patients lived alone and 70 patients lived together with his/her spouse. In the Macao group, there were 65 males and 54 females with an average age of  $67.08 \pm 13.192$  years; 17 patients lived alone and 102 patients lived together with his/her spouse. The age and the male-to-female ratio in the Beijing group were higher than those in the Macao group ( $P < 0.05$ ). There was no significant difference in smoking history ( $P = 0.136$ ) or the number of cigarettes smoked ( $P = 0.180$ ) between the two groups. The length of smoking history in the Beijing group was significantly longer than that in the Macao group

( $P = 0.010$ ). The incidence rates of tumors, hypertension, hyperlipidemia, renal dysfunction, peripheral neuropathy, and retinopathy were significantly higher in the Beijing group than in the Macao group ( $P < 0.01$ ). These results are summarized in detail in Tables 1 and 2.

TG, TC, LDL-C, Cr, LVID, LVEDD, and the incidence of segmental wall motion abnormalities were significantly higher in the Macao group than in the Beijing group ( $P < 0.05$ ). However, fasting blood glucose, postprandial blood glucose, and LVEF were significantly lower in the Macao group than in the Beijing group ( $P < 0.05$ ). These results are provided in detail in Table 3.

The age of diabetic foot disease onset was significantly lower in the Macao group than in

**Table 2** Concomitant diseases in patients with DM

Concomitant disease	Total ( <i>n</i> = 243)	Beijing group ( <i>n</i> = 124)	Macao group ( <i>n</i> = 119)	$\chi^2$ value	<i>P</i> value
Tumor	24 (9.9%)	3 (2.4%)	21 (17.6%)	15.819	< 0.001
Hypertension	179 (73.7%)	82 (66.1%)	97 (81.5%)	7.407	0.006
Hyperlipidemia	102 (42.0%)	16 (12.9%)	86 (72.3%)	87.867	< 0.001
Coronary heart disease	67 (27.6%)	27 (21.8%)	40 (33.6%)	3.713	0.054
Stroke	52 (21.4%)	22 (17.7%)	30 (25.2%)	2.014	0.156
Renal dysfunction	65 (26.7%)	7 (5.6%)	58 (48.7%)	57.555	< 0.001
Peripheral neuropathy	37 (20.8%)	2 (3.4%)	34 (29.4%)	16.221	< 0.001
Retinopathy	57 (34.3%)	6 (9.8%)	51 (48.6%)	25.677	< 0.001

the Beijing group ( $P = 0.026$ ). The durations of DM and diabetic foot disease as well as the time taken to progress to diabetic foot disease were significantly shorter in the Macao group than in the Beijing group, and the ankle-brachial index was higher in the Macao group (all  $P < 0.05$ ). These results are summarized in detail in Table 4.

In the Beijing group, the surgical treatment rate was 96.0%, which was significantly higher than that in the Macao group (21.0%) ( $P < 0.001$ ) (Table 5). A total of 36 patients died, and cardiac failure was the most common cause (72.2%). There was no significant difference in the mortality rate ( $P = 0.114$ ) or cause of death ( $P = 0.883$ ) between the Beijing group and the Macao group (Table 6).

Multivariate linear regression analysis showed that total monthly household income and smoking history were independent risk factors associated with the onset age of diabetic foot disease (Tables 7, 8). Additionally, the onset age of DM and the length of smoking history were independent risk factors associated with the progression time of diabetic foot disease (Tables 9, 10). Moreover, the severity of diabetic foot disease was categorized into four groups according to the degree of vascular stenosis: mild (25–49%), moderate (50–74%), severe (75–99%), and occlusion (100%) (Table 11). Multivariate linear regression analysis revealed that age, the clinical course of diabetic foot disease, and length of smoking history were independent risk factors associated

with the severity of diabetic foot disease (Tables 12, 13). Kaplan–Meier analysis showed that the survival time was significantly longer in the Beijing group than in the Macao group ( $P = 0.002$ ) (Fig. 1). Cox regression analysis showed that renal dysfunction and APTT were independent risk factors associated with the survival time of patients with diabetic foot disease (Tables 14, 15).

## DISCUSSION

The patients in the Beijing group were older than those in the Macao group, and the patients in the Macao group had more comorbidities during the early stage of DM. These findings indicate that the prevention and treatment services in Beijing are better than those in Macao. Further analyses revealed that hyperlipidemia, renal dysfunction, and cardiac dysfunction are more common in Macao than in Beijing, which may be related to differences in dietary patterns and lifestyles as well as inadequate education in Macao. During previous work, we found that residents in Macao have a lack of knowledge regarding the prevention and treatment of DM, and that irregular blood glucose monitoring and untimely treatment severely impair public health in Macao. In patients with DM, poor capillary perfusion affects wound healing and the formation of collateral circulation. Additionally, arterial occlusion aggravates the perfusion deficiency in

**Table 3** Laboratory results in patients with DM

Variable	Total ( <i>n</i> = 243)	Beijing group ( <i>n</i> = 124)	Macao group ( <i>n</i> = 119)	Statistical value	<i>P</i> value
Serum lipid levels					
TG (mmol/L) <sup>a</sup>	2.28 ± 1.482	1.82 ± 1.151	2.77 ± 1.631	− 5.230	< 0.001
TC (mmol/L) <sup>a</sup>	5.07 ± 1.713	4.53 ± 1.187	5.62 ± 1.985	− 5.144	< 0.001
LDL-C (mmol/L) <sup>a</sup>	2.88 ± 1.265	2.71 ± 1.005	3.06 ± 1.473	− 2.131	0.034
HDL-C (mmol/L) <sup>a</sup>	1.09 ± 0.353	1.06 ± 0.300	1.12 ± 0.399	− 1.379	0.169
Renal function					
Cr (mmol/L) <sup>b</sup>	120.34 ± 128.697	101.54 ± 119.931	139.93 ± 134.969	− 5.155	< 0.001
BUN (mmol/L) <sup>b</sup>	7.66 ± 8.466	8.19 ± 10.877	7.12 ± 4.805	− 0.207	0.836
Positive urine protein <sup>c</sup>	155 (64.3%)	84 (67.7%)	71 (60.7%)	1.307	0.253
Blood glucose levels					
Fasting blood glucose (mmol/L) <sup>a</sup>	8.29 ± 2.913	8.86 ± 2.463	7.94 ± 3.121	2.161	0.032
Postprandial blood glucose (mmol/L) <sup>a</sup>	11.64 ± 3.759	12.76 ± 3.422	10.94 ± 3.804	3.345	0.001
Cardiac function parameters					
LVID (mm) <sup>a</sup>	37.48 ± 6.877	35.85 ± 5.214	44.63 ± 8.652	19.271	< 0.001
LVEDD (mm) <sup>a</sup>	47.39 ± 7.220	45.89 ± 6.273	53.22 ± 7.797	6.369	0.013
LVEF (%) <sup>a</sup>	66.47 ± 10.851	67.30 ± 8.171	53.03 ± 12.834	17.665	< 0.001
Segmental wall motion abnormalities ( <i>n</i> ) <sup>c</sup>	16 (11.6%)	7 (6.7%)	9 (27.3%)	10.401	0.001

<sup>a</sup> Independent-sample *t* test<sup>b</sup> Rank sum test<sup>c</sup> Chi-square test

distal limbs, and neuropathy makes patients insensitive to pain [7]. Moreover, DM prevention is insufficiently publicized, and patients have limited access to relevant knowledge about DM. Macao has limited medical resources but a large number of patients with DM. In contrast to patients in Beijing, short-term follow-up monitoring of DM patients is impossible in Macao. Most patients return to the clinic more than half a year after taking medicine. During this period, their blood glucose levels are not regularly monitored. Medical resources during hospitalization are also more limited in Macao, so the management of DM is usually delayed.

Furthermore, Macao lacks specialists such as vascular surgeons and orthopedic surgeons, and diabetic foot diseases cannot be promptly managed. General practitioners in the community health center lack relevant professional knowledge, so DM and diabetic foot disease are usually underdiagnosed. As a result of these factors, diabetic foot disease occurs in younger populations and progresses more rapidly in Macao than in Beijing.

DM is an independent risk factor for the occurrence and development of arteriosclerosis. Vascular sclerosis in DM patients is more severe than that in non-DM patients. The leading



**Table 4** Clinical characteristics of diabetic foot disease

Characteristic	Total ( <i>n</i> = 243)	Beijing group ( <i>n</i> = 124)	Macao group ( <i>n</i> = 119)	Statistical value	<i>P</i> value
DM					
Onset age (years) <sup>a</sup>	55.86 ± 12.753	55.37 ± 11.411	56.37 ± 14.047	− 0.609	0.543
Duration (years) <sup>a</sup>	13.15 ± 8.064	15.49 ± 8.159	10.71 ± 7.224	4.834	< 0.001
Diabetic foot disease					
Onset age (years) <sup>a</sup>	65.51 ± 11.358	67.10 ± 9.243	63.85 ± 13.040	2.237	0.026
Duration (months) <sup>b</sup>	40.18 ± 28.622	44.48 ± 30.726	35.69 ± 25.617	1.735	0.028
Progression time of diabetic foot disease (years) <sup>b</sup>	9.65 ± 7.797	11.73 ± 8.067	7.48 ± 6.894	4.412	< 0.001
Left ankle ABI <sup>a</sup>	0.62 ± 0.273	0.57 ± 0.249	0.68 ± 0.286	− 3.222	0.001
Right ankle ABI <sup>a</sup>	0.67 ± 0.306	0.63 ± 0.303	0.72 ± 0.304	− 2.363	0.019
Affected lower extremity <sup>c</sup>					
Left lower extremity	103 (42.7%)	73 (59.8%)	30 (25.2%)	54.205	< 0.001
Right lower extremity	58 (24.1%)	35 (28.7%)	23 (19.3%)		
Bilateral lower extremities	80 (33.2%)	14 (11.5%)	66 (55.5%)		
Severity of diabetic foot disease on the left leg <sup>b</sup>					
Mild (25–49%)	43 (17.7%)	12 (9.7%)	31 (26.1%)	− 4.380	< 0.001
Moderate (50–74%)	48 (19.8%)	14 (11.3%)	34 (28.6%)		
Severe (75–99%)	110 (45.3%)	74 (59.6%)	36 (30.3%)		
Occlusion	42 (17.3%)	24 (19.4%)	18 (15.1%)		
Severity of diabetic foot disease on the right leg <sup>b</sup>					
Mild (25–49%)	73 (30.0%)	38 (30.6%)	35 (29.4%)	− 0.654	0.513
Moderate (50–74%)	48 (19.8%)	16 (12.9%)	32 (26.9%)		
Severe (75–99%)	76 (31.3%)	48 (38.7%)	28 (23.5%)		
Occlusion	46 (18.9%)	22 (17.7%)	24 (20.2%)		
Clinical symptoms <sup>b</sup>					
Asymptomatic	12 (4.9%)	5 (4.0%)	7 (5.9%)	− 1.766	0.077
Intermittent claudication	116 (47.7%)	57 (46.0%)	59 (49.6%)		
Rest pain	57 (23.5%)	23 (18.5%)	34 (28.6%)		
Ulceration and gangrene	58 (23.9%)	39 (31.5%)	19 (16.0%)		

ABI ankle-brachial index

<sup>a</sup> Independent-sample *t* test<sup>b</sup> Rank sum test<sup>c</sup> Chi-square test

**Table 5** Treatment modalities of diabetic foot disease

Treatment modality	Total ( <i>n</i> = 243)	Beijing group ( <i>n</i> = 124)	Macao group ( <i>n</i> = 119)	$\chi^2$ value	<i>P</i> value
Surgical treatment	144 (59.3%)	119 (96.0%)	25 (21.0%)	141.328	< 0.001
Balloon dilatation	77 (31.7%)	53 (42.7%)	24 (20.2%)	14.295	< 0.001
Stent implantation	105 (43.2%)	82 (66.1%)	23 (19.3%)	54.203	< 0.001
Catheter thrombolysis	17 (7.0%)	17 (13.7%)	0 (0.0%)	17.542	< 0.001
Amputation	20 (8.2%)	20 (16.1%)	0 (0.0%)	20.915	< 0.001
Pharmacotherapy	221 (90.9%)	103 (83.1%)	118 (99.2%)	19.105	< 0.001
Biguanides	66 (27.2%)	15 (12.1%)	51 (42.9%)	29.043	< 0.001
Sulfonylureas	47 (19.3%)	8 (6.5%)	39 (32.8%)	26.968	< 0.001
Insulin	124 (51.0%)	50 (40.3%)	74 (62.2%)	11.614	0.001
Acarbose	33 (13.6%)	28 (22.6%)	5 (4.2%)	17.478	< 0.001

**Table 6** Cause of death in patients with diabetic foot disease

Cause of death	Total ( <i>n</i> = 36)	Beijing group ( <i>n</i> = 14)	Macao group ( <i>n</i> = 22)	$\chi^2$ value	<i>P</i> value
Cardiac failure	26 (72.2%)	10 (71.4%)	16 (72.7%)	2.578	0.883
Respiratory failure	6 (16.7%)	2 (14.3%)	4 (18.2%)		
Uremia	1 (2.8%)	1 (7.1%)	0 (0.0%)		
Septicemia	2 (5.6%)	1 (7.1%)	1 (4.5%)		
Cerebral hemorrhage	1 (2.8%)	0 (0.0%)	1 (4.5%)		

cause of death was cardiac failure in both groups, suggesting that cardiac dysfunction is common in patients with diabetic foot disease. The surgical treatment rate was higher in the Beijing group; existing evidence has shown that early surgery or interventional therapy can promote wound healing [7]. Surgical treatment can obviously improve the blood supply to the lower extremities, increasing blood perfusion of the foot and improving the local oxygen supply. More patients received pharmacotherapy in Macao, which may be related to the referral appointment system used there. The clinicians' lack of knowledge and an absence of multidisciplinary cooperation also contribute to the high rate of drug treatment in Macao. Wound

healing is multifactorial, and wound nursing should be emphasized.

Smoking is a risk factor for the occurrence and development of diabetic foot disease. Smoking can significantly reduce the onset age and aggravate the severity of diabetic foot disease, and short-term smoking (length of smoking history < 30 years) can also shorten the progression time of diabetic foot disease. Our study also showed that household income was negatively correlated with onset age. We speculate that these results may be attributed to differences in lifestyle between the two cities. Therefore, the prevention of DM and diabetic foot disease needs to be encouraged in the Macao population. Healthy lifestyles and family



**Table 7** Univariate analysis of factors associated with the onset age of diabetic foot disease

Variate	Regression coefficient ( <i>b</i> )	Standardized regression coefficient ( $\beta$ )	<i>t</i> value	<i>P</i> value	95% CI
District (Beijing, Macao)	− 3.256	− 0.144	− 2.253	0.025	− 6.103, − 0.409
Gender	− 3.023	− 0.130	− 2.030	0.043	− 5.957, − 0.089
Income	− 3.875	− 0.250	− 3.912	< 0.001	− 5.826, − 1.923
Marital status	− 3.697	− 0.148	− 2.328	0.021	− 6.824, − 0.569
Insulin usage	− 3.117	− 0.137	− 2.155	0.032	− 5.967, − 0.267
Smoking history	− 4.353	− 0.190	− 3.009	0.003	− 7.203, − 1.503

Only statistically significant variates are presented

**Table 8** Multivariate linear regression analysis of factors associated with the onset age of diabetic foot disease

Variate	Regression coefficient ( <i>b</i> )	Standardized regression coefficient ( $\beta$ )	<i>t</i> value	<i>P</i> value	95% CI
Income	− 3.916	− 0.253	− 4.044	< 0.001	− 5.824, − 2.008
Smoking history	− 4.895	− 0.212	− 3.395	0.001	− 7.737, − 2.054

Only statistically significant variates are presented

**Table 9** Univariate analysis of factors associated with the progression time of diabetic foot disease

Variate	<i>B</i> value	Standard error	Wald	<i>P</i> value	95% CI	Exp( <i>B</i> ) 95% CI
Length of smoking history						
0 years	− 0.580	0.145	15.882	< 0.001	− 0.865, − 0.295	0.560 (0.421, 0.745)
1–30 years	− 1.762	0.196	80.822	< 0.001	− 2.146, − 1.378	0.172 (0.117, 0.252)
> 31 years	0	–	–	–	–	–
District						
Beijing	1.146	0.251	20.859	< 0.001	0.654, 1.637	3.144 (1.363, 7.255)
Macao	0	–	–	–	–	–
Education level						
≤ Elementary school	− 1.220	0.176	48.226	< 0.001	− 1.565, − 0.876	0.295 (0.209, 0.416)
< Junior college	− 1.362	0.174	61.039	< 0.001	− 1.703, − 1.020	0.256 (0.182, 0.361)
≥ Junior college	0	–	–	–	–	–
TG (mmol/L)	− 0.226	0.088	6.563	0.010	− 0.398, − 0.053	0.798 (0.671, 0.948)
TC (mmol/L)	− 0.203	0.071	8.203	0.004	− 0.343, − 0.064	0.816 (0.710, 0.938)
RBC ( $\times 10^{12}/L$ )	− 0.342	0.088	15.021	< 0.001	− 0.515, − 0.169	0.710 (0.598, 0.844)
PLT ( $\times 10^9/L$ )	− 0.004	0.014	6.462	0.011	0.001, 0.006	1.004 (1.001, 1.006)
Income (10,000 yuan)	− 0.639	0.242	7.002	0.008	− 1.113, − 0.166	0.528 (0.329, 0.847)

Only statistically significant variates are presented

**Table 10** Multivariate linear regression analysis of factors associated with the progression time of diabetic foot disease

Variate	B value	Standard error	Wald	P value	95% CI	Exp(B) 95% CI
(0–3 years): ( $\geq$ 4 years)	– 6.687	1.003	44.420	< 0.001	– 8.654, – 4.721	0.001 (0.000, 0.009)
(0–10 years): ( $\geq$ 11 years)	– 4.092	0.925	19.555	< 0.001	– 5.905, – 2.278	0.017 (0.003, 0.102)
Onset age (years)	– 0.080	0.013	37.140	< 0.001	– 0.106, – 0.054	0.923 (0.899, 0.947)
Length of smoking history						
0 years	0.008	0.359	0.001	0.982	– 0.695, 0.712	1.008 (0.499, 2.037)
1–30 years	– 1.445	0.487	8.789	0.003	– 2.400, – 0.490	0.236 (0.091, 0.613)
$\geq$ 31 years	0	–	–	–	–	–

Only statistically significant variates are presented

**Table 11** Severity of diabetic foot disease

Severity	Right leg				Total
	Mild	Moderate	Severe	Occlusion	
Left leg					
Mild	8	14	12	9	43
Moderate	19	17	10	2	48
Severe	37	13	44	16	110
Occlusion	9	4	10	19	42
Total	73	48	76	46	243

care are crucial to reducing the incidence of diabetic foot disease. Age was positively correlated with the progression and severity of diabetic foot disease. With the increase of age, the risk factors of arteriosclerosis and DM increase the probability of infection.

Renal dysfunction and blood coagulation dysfunction can adversely affect the survival time of patients with diabetic foot disease. Renal dysfunction is a severe and common complication of DM. The incidence of renal dysfunction is much higher in Macao, and many patients require early dialysis. Frequent dialysis significantly reduces patient quality of life. Arteriosclerosis is more serious in DM patients who undergo dialysis. Both DM and uremia can lead to neuropathy, resulting in a refractory wound that does not heal for a long

time. Local wound infection can be associated with pain, swelling, and exudation, affecting the utilization of the lower extremities and further reducing quality of life. Most patients have multiple complications, especially arteriosclerosis-related ischemic diseases such as coronary heart disease and cerebral arteriosclerosis, significantly increasing the risk of cardiac failure. In the current study, cardiac failure was the leading cause of death in both groups. Additionally, chronic consumption reduced the immunity of patients and increased the risk of systemic infection. Lung infection also accounted for a large proportion of the deaths in the two groups. Therefore, the benefits of improving renal function and blood coagulation function should be highlighted in the treatment of diabetic foot disease.

**Table 12** Univariate analysis of factors associated with the severity of diabetic foot disease

Variate	<i>B</i> value	Standard error	95% CI	Wald	<i>P</i> value	Exp( <i>B</i> ) 95% CI
Age	0.030	0.009	0.012, 0.048	10.574	0.001	1.030 (1.012, 1.049)
District						
Beijing	0.961	0.200	0.568, 1.354	22.998	< 0.001	2.615 (1.765, 3.874)
Macao	0	–	–	–	–	–
Length of smoking history						
0 years	– 1.325	0.260	– 1.835, – 0.815	25.923	< 0.001	0.266 (0.160, 0.443)
1–30 years	– 1.597	0.362	– 2.307, – 0.887	19.417	< 0.001	0.203 (0.100, 0.412)
≥ 31 years	0	–	–	–	–	–
Systolic pressure	0.012	0.005	0.002, 0.022	5.162	0.023	1.012 (1.002, 1.022)
Marital status						
Single/divorced/widowed	0.844	0.223	0.407, 1.281	14.348	< 0.001	2.326 (1.503, 3.601)
Married/cohabiting	0	–	–	–	–	–
ALT (U/L)	– 0.014	0.005	– 0.025, – 0.004	6.903	0.009	0.986 (0.976, 0.996)
RBC ( $\times 10^{12}/L$ )	– 0.313	0.082	– 0.474, – 0.153	14.603	< 0.001	0.731 (0.623, 0.859)
PLT ( $\times 10^9/L$ )	0.005	0.001	0.003, 0.008	15.194	< 0.001	1.005 (1.003, 1.008)
Income (10,000 yuan)	– 0.440	0.212	– 0.855, – 0.026	4.333	0.037	0.644 (0.425, 0.975)
Clinical course of diabetic foot disease (years)	0.011	0.004	– 0.004, – 0.018	8.628	0.003	1.011 (1.004, 1.018)

Only statistically significant variates are presented

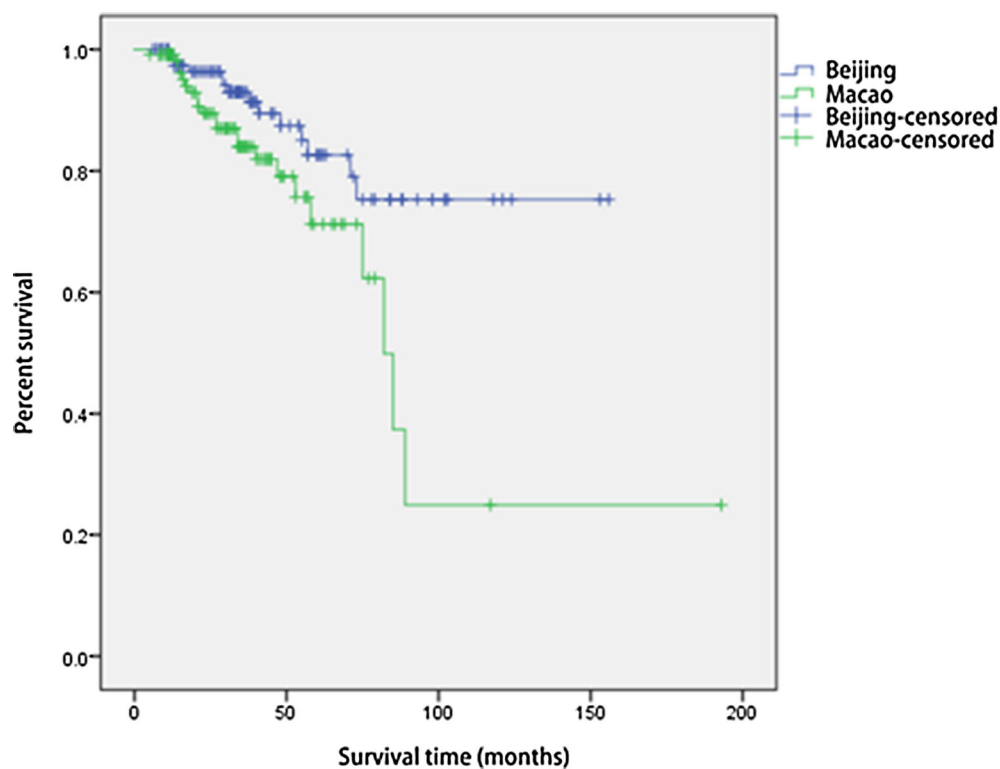
Currently, the prevention and treatment of diabetic foot disease is an important health care issue around the world [8, 9]. Better health care services and management are greatly beneficial for patients with DM. Therefore, it is recommended that health education should be

strengthened and popularized, the hierarchical management of DM and diabetic foot disease should be instituted [3, 8, 10], and a standardized evaluation system should be established, including early diagnosis of diabetic foot disease (skin condition, toenail condition, foot

**Table 13** Multivariate linear regression analysis of factors associated with the severity of diabetic foot disease

Variate	<i>B</i> value	Standard error	95% CI	Wald	<i>P</i> value	Exp( <i>B</i> ) 95% CI
Age	0.031	0.011	0.010, 0.052	8.175	0.004	1.032 (1.010, 1.054)
Clinical course of diabetic foot disease (years)	0.009	0.004	0.001, 0.017	5.226	0.022	1.009 (1.001, 1.017)
Length of smoking history						
0 years	− 1.468	0.291	− 2.038, − 0.898	25.451	< 0.001	0.230 (0.130, 0.408)
1–30 years	− 1.144	0.378	− 1.884, − 0.403	9.168	0.002	0.319 (0.152, 0.668)
≥ 31 years	0	–	–	–	–	–

Only statistically significant variates are presented



**Fig. 1** Kaplan–Meier analysis showed that the average survival time in the Beijing group (129.306 months; 95% confidence interval: 116.101–142.511 months) was significantly longer than that in the Macao group (96.700 months; 95% confidence interval: 64.684–128.717 months)

**Table 14** Univariate analysis of factors associated with the survival time of patients with diabetic foot disease

Variate	<i>B</i> value	Standard error	Wald	<i>P</i> value	HR	95% CI
District						
Beijing	0	–	–	–	–	–
Macao	0.922	0.355	6.727	0.009	2.514	1.253, 5.046
Occupation						
Primary industry			4.483	0.214		
Secondary industry	– 1.949	1.323	2.502	0.114	0.142	0.013, 1.593
Tertiary industry	– 1.677	0.832	4.060	0.044	0.187	0.037, 0.955
Others	– 1.344	0.752	3.191	0.074	0.261	0.060, 1.140
Hyperlipidemia	0.795	0.347	5.260	0.022	2.214	1.123, 4.367
Renal dysfunction	1.553	0.346	20.191	< 0.001	4.724	2.400, 9.299
Cr (mmol/L)	0.003	0.001	28.713	< 0.001	1.003	1.002, 1.004
BUN (mmol/L)	0.051	0.011	19.949	< 0.001	1.053	1.029, 1.077
Stent implantation	– 0.957	0.387	6.110	0.013	0.384	0.180, 0.820
AST (U/L)	0.009	0.004	4.869	0.027	1.009	1.001, 1.017
HGB (g/L)	– 0.035	0.009	14.041	0.001	0.966	0.949, 0.984
PLT ( $\times 10^9$ /L)	– 0.006	0.002	7.044	0.008	0.994	0.990, 0.998
APTT (s)	0.046	0.013	13.337	< 0.001	1.047	1.022, 1.073
Positive urine protein	1.078	0.362	8.858	0.003	2.940	1.445, 5.980

Only statistically significant variates are presented

**Table 15** Multivariate linear regression analysis of factors associated with the survival time of patients with diabetic foot disease

Variate	<i>B</i> value	Standard error	Wald	<i>P</i> value	HR	95% CI
Renal dysfunction	1.720	0.372	21.421	0.003	5.584	2.696, 11.569
APTT	0.058	0.015	15.473	0.001	1.060	1.029, 1.090

Only statistically significant variates are presented

deformity, etc.), evaluation of lower-limb blood vessels (artery ultrasound or CTA), and neurological assessments (sensory disturbance or motor abnormalities) [5, 11]. Furthermore, multidisciplinary cooperation in the treatment of diabetic foot disease and the establishment of a follow-up system that can provide a long-term individualized management strategy are important [12–14].

There are some limitations of this study. Firstly, all subjects were enrolled from local hospitals, so selection bias was unavoidable. Secondly, this was a retrospective case–control study, so there may be recall bias. Thirdly, the sample size was limited. In the future, a prospective multicenter study is warranted.

## CONCLUSIONS

We found that smoking was a risk factor for the occurrence and development of diabetic foot; it significantly reduced the onset age and aggravated the severity of this disease. The onset age of diabetic foot was lower in high-income patients, and prevention should be encouraged in this population. Elderly age may be associated with a rapidly developing and severe diabetic foot. The clinical course was also associated with the severity of diabetic foot. Renal and coagulation function should be closely monitored during the treatment of diabetic foot.

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**Compliance with Ethics Guidelines.** The trial was conducted in accordance with the Declaration of Helsinki, the International Conference on Harmonisation guidelines for good clinical practice, and all applicable laws and regulations. This study was approved by the Ethics Committee of Beijing Chaoyang Hospital. Written informed consent was obtained from each participant.

**Data Availability.** The datasets obtained and/or analyzed during the current study are available from the corresponding author on reasonable request.

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