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Research Article

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Analysis of Influencing Factors of Diabetic Foot Minor Amputation

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Abstract

Objective: *To investigate the factors that influence diabetic foot (DF) minor amputation. Methods: In this case-control study, the clinical data of 955 hospitalized patients with DF were retrospectively analyzed, according to whether hospitalization amputation was divided into minor amputation and the non-amputation group, compared two groups of general data, laboratory examination, diabetes complications and complications, such as differences, multiple factors regression analysis DF Risk factors associated with minor amputation in patients. Results: There were statistically significant differences between the two groups in DPN, DR, PAD, ABI, TBI, and Wagner grades, as well as age, sex, HbA1c, FPG, Scr, SUA, TC, ALB, HDL-C, WBC, and Hb (P<0.05). The logistic regression analysis that HbA1c (odds ratio [OR] 1.082 [95% CI 1.011–1.158], p= 0.023), ABI < 0.9 (odds ratio [OR] 1.793 [95% CI 1.316–2.443], p=0.000), TBI < 0.7(odds ratio [OR] 2.569 [95% CI 1.889–3.495], p=0.000), Wagner classification (odds ratio [OR] 2.792 [95% CI 2.303–3.384], p=0.000) and PAD (odds ratio [OR] 2.343 [95% CI 1.731–3.170], p=0.000) were significant risk factors for DF minor amputation (P < 0.05). Higher Hb (odds ratio [OR] 0.981 [95% CI 0.973–0.988], p=0.000) was an independent protective factor for minor amputation. Conclusion: HbA1c, lower ankle brachial index level, and lower toe-brachial index level were all related with minor amputation. Wagner classification and diabetic peripheral angiopathy may represent a novel independent factor. In light of these concerns, early preventive and timely multidisciplinary assistance is critical to prevent diabetic foot minor amputation.*

Keywords: diabetic foot, minor amputation

1. Introduction

Diabetes has become a global issue due to the rising number of diabetic patients. Diabetes has a global incidence of 8.8 % in 2017 and is expected to rise to 9.9 % by 2045 [1]. Diabetic foot (DF) is a common complication of diabetes. The lifetime prevalence of diabetic foot ulcers has been estimated to be between 19 and 34% in diabetic patients [2]. In addition, the annual incidence rates of diabetic foot ulcers in the global population of diabetic patients have been reported to be 6.3 percent [3]. Diabetic foot is frequently accompanied with peripheral neuropathy and vascular disease, resulting in long-term loss of nourishment on the wound surface and making regeneration difficult. These open Sexual wounds are conducive to pathogen invasion and are prone to serious infection [4]. Without timely and appropriate intervention, patients will face the risk of amputation. According to research, the diabetic foot amputation rate is the highest among non-traumatic amputations [5]. The mortality rate of patients after amputation was as high as 1.00%-13.00% [6]. Amputation of DF patients not only results in the loss of some functions and the development of some deformities, but it may also result in major psychological disorders and have a negative impact on the patients' quality of life. Minor amputations at or below the ankle level are classified as minor amputations, whereas amputations above the ankle level are classified as major amputations. This study aims to provide evidence for clinical diagnosis and treatment of DF by exploring the influencing factors of DF minor amputation.

2. Methods

2.1 Study Populations

A retrospective analysis was performed on 955 patients with DF hospitalized in the endocrinology department of the Air Force Medical Center, PLA from December 2016 to April 2021. Participants included 692 males and 263 females. All the included subjects met the definition of DF established by the World Health Organization in 1999: “In patients with diabetes mellitus, infection, ulceration, and/or deep tissue destruction of the lower extremity are caused by the concomitant neuropathy and various degrees of vascular diseases” [7]. Amputation of a toe or half foot as a con-

sequence of DF surgery or excision of a necrotic limb due to local irreversible gangrene is diagnostic criteria for small amputation. The diabetic foot was graded after the wound was examined using the Wagner classification of diabetic foot, which is as follows [8]:
(1) Grade 0: No open lesions; may have deformity or cellulitis.
(2) Grade 1: Superficial diabetic ulcer (partial or full thickness).
(3) Grade 2: Ulcer extension to the ligament, tendon, joint capsule, or deep fascia without abscess or osteomyelitis.
(4) Grade 3: Deep ulcer with abscess, osteomyelitis, or joint sepsis.
(5) Grade 4: Gangrene localized to the portion of the forefoot or heel.
(6) Grade 5: Extensive gangrenous involvement of the entire foot.

The exclusion criteria were as follows:
(1) Patients who are unable to complete relevant examinations; (2) Patients with liver and kidney dysfunction; (3) Patients with acute complications of DM; (4) Pregnant and lactating women; (5) Patients with malignant tumors;

2.2 Data Collection

2.2.1 The General Information: gender, age, body mass index (BMI), smoking history, Drinking history, hypertension history, hyperlipidemia history, coronary heart disease history, duration of diabetes mellitus, duration of diabetes foot, peripheral arterial disease (PAD), Diabetic peripheral neuropathy (DPN), diabetic retinopathy (DR) and diabetic nephropathy (DN).

2.2.2 Laboratory Inspection: glycerogelatin hemoglobin (HbA1c), fasting plasma glucose (FPG), vitamin D, total cholesterol(TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), Blood urea nitrogen (BUN), Serum creatinine (Scr), serum uric acid (SUA), albumin (ALB), white blood cell count (WBC) and hemoglobin (Hb). After fasting for 8 hours, blood samples were drawn from the patients. All blood biomarkers were tested in the same laboratory.

2.2.3 Relevant Clinical Examination: Toe-Brachial Index (TBI) and Ankle Brachial Index (ABI). TBI Detection Method: TBI was measured using the network arteriosclerosis detection equipment BP-203RPE III (Omron, Japan). The subject was measured while laying calmly for 10 to 15 minutes. A small cuff was tied at the brachial artery and the thumb of the bilateral upper arm of the patient, and relevant parameters were input, and the instrument automatically calculated TBI. The low values in the left and right sides of the patient were taken at the patient's TBI, and TBI<0.7 was regarded as the outlier [9]. ABI detection methods are as follows: ABI of all patients was detected by color Doppler ultrasonography with a probe frequency of 8-10 MHz. The probe was placed in the pulse position of the patient at an Angle of 45°-60° from the skin, and the probe was moved until the clearest signal was presented. When the blood flow signal disappeared, the cuff was progressively inflated until the pressure was more than 20 mmHg (1 mmHg=0.133 kPa), and then gently deflated and the blood pressure was measured when the blood flow signal reappeared. The blood pressure of both arms was measured and the systolic blood pressure on the higher side was taken as the upper arm systolic blood pressure. The mean blood pressure of the ipsilateral posterior tibial artery and dorsal foot artery was taken as the ankle systolic blood pressure. ABI= ankle systolic blood pressure/upper arm systolic blood pressure. ABI < 0.9 was considered as abnormal ABI.

2.3 Statistical Analyses

SPSS Statistics 23.0 software packages were used to conduct the data analysis. Variables with normal distribution were expressed as mean ± standard deviation, and the t test was used to compare the two groups. Variables with non-normal distribution were expressed as median (quartile spacing), and the non-parametric Mann–Whitney U-test was used for comparison between the groups. Counting data were expressed as a percentage. Comparison between the two groups was conducted by x2 test. The independent factors were analyzed by binary logistic regression. Before regression analysis, the independent variables of non-normal distribution were transformed by square root or logarithm. $P < 0.05$ was considered statistically significant.

3. Results

3.1 Comparison of General Clinical Data Between the Two Groups

Table 1 shows general clinical data of 955 patients in the two groups. In the present study. The number of patients with DPN, DR, and PAD, as well as those with minor amputations, was greater in the current research ($P<0.05$) than in the non-amputation group. The ABI and TBI levels were significantly lower in the minor amputation group compared to the non-amputation group ($P <0.05$). Wagner grading revealed a statistically significant difference ($P<0.05$) between the two groups. However, smoking history, drinking history, hypertension history, coronary heart disease history, hyperlipidemia history, and DN were not statistically significant ($p>0.05$).

Table 1: Comparison of general data between DF groups with and without minor amputation

Item	Non-amputation(n=520)	minor amputation(n=435)	t/x2	P-value
Smoking history(yes/no,n/n)	230/290	181/254	0.664	0.227
Drinking history(yes/no,n/n)	174/346	136/299	0.522	0.257
Hypertension history(yes/no,n/n)	306/214	250/185	0.184	0.358
Coronary heart disease history				
(yes/no,n/n)	144/376	106/329	1.355	0.138
Hyperlipidaemia history (yes/no,n/n)	172/157	348/278	0.953	0.182
DPN	453/67	409/26	12.858	0.000
DR	270/250	275/160	12.334	0.000
PAD	205/315	241/194	24.297	0.000
DN	254/266	236/199	2.771	0.055
ABI(≥0.9/ < 0.9)	283/237	197/238	7.908	0.003
TBI(≥0.9/ < 0.7)	258/262	144/291	11.299	0.000
Wagner classification(n)			150.022	0.000
0	12(2.3%)	0		
1	42(8.1%)	2(0.5%)		
2	102(19.6%)	25(5.7%)		
3	157(30.2%)	73(16.8%)		
4	200(38.5%)	327(75.2%)		
5	7(1.3%)	8(1.8%)		

3.2 Comparison of Patient Clinical Characteristics of The 2 Groups

Compared with the non-amputation group, the minor amputation group was more male, and had higher Age, HbA1c, FPG, HDL-C and WBC((P<0.05). Scr, SUA, TC, ALB, and Hb levels in the minor amputation group were significantly lower than in the non-amputation group (P <0.05). No significant difference in other indices was detected (P>0.05, Table 2).

Table 2: Comparison of clinical and biochemical data between DF groups with and without minor amputation.

Item	Non-amputation(n=520)	minor amputation(n=435)	t/x2/Z	P-value
Age (yr)	60.36±10.56	62.61±11.31	1.934	0.002
Gender(Male/Female)	388/132	304/131	0.256	0.060
DM duration(yr)	6.0(4.92,14.75)	5.75(4.67,16.0)	1.291	0.256
DF duration(yr)	2.0(1.0,4.0)	2.0(0.87,6.00)	1.146	0.284
BMI (kg/m2)	24.39±3.94	24.47±3.61	0.239	0.752
HbA1c(%)	8.67±2.15	9.06±2.20	0.001	0.006
FPG(mmol /L)	7.5(5.9,10.28)	8.2(6.3,10.6)	6.676	0.010
Scr(mol /L)	72(59,97)	70(55,88)	5.664	0.017
SUA(mmol /L)	303(230.25,377.75)	275(218,355)	9.886	0.002
TC(mmol /L)	3.98(3.35,4.73)	3.88(3.16,4.58)	6.330	0.013
TG(mmol /L)	1.29(0.98,1.79)	1.23(0.93,1.78	2.038	0.153
HDL-C(mmol /L)	0.93(0.79,1.11)	1.0(0.83,1.21)	17.160	0.000
LDL-C(mmol /L)	2.39(1.82,2.90)	2.29(1.79,2.9)	0.727	0.394
ALT (U/L)	14.0(10,21)	14(10,22)	0.277	0.599
AST(U/L)	17(14,22)	18(14,24)	0.696	0.404
Alb(g/L)	39(35,41.5)	37(33,40)	22.046	0.000
WBC(×109/L)	6.80(5.50,8.83)	7.40(5.80,9.7)	8.355	0.004
Hb(g /L)	119.21±19.09	112.49±21.86	1.015	0.000

3.3 Influence Factors of Df Minor Amputation

For logistic regression analysis, the presence or absence of minor amputation was utilized as the dependent variable, while statistically significant indicators were employed as independent variables. The results showed that HbA1c (odds ratio [OR] 1.082 [95% CI 1.011–1.158], p=0.023), ABI < 0.9 (odds ratio [OR] 1.793 [95% CI 1.316–2.443], p = 0.000), TBI < 0.7 (odds ratio [OR] 2.569 [95% CI 1.889–3.495], p=0.000), Wagner classification (odds ratio [OR] 2.792 [95% CI 2.303–3.384], p=0.000) and PAD (odds ratio [OR] 2.343 [95% CI 1.731–3.170], p=0.000) were significant risk factors for DF minor amputation (P < 0.05). Higher Hb (odds ratio [OR] 0.981 [95% CI 0.973–0.988], p=0.000) was an independent protective factor for minor amputation (P < 0.05, Table 3).

Table 3: Analysis of influencing factors of DF minor amputation.

Variable	*β*	*SE*	*Waldχ2*	*P*	*OR*	*95% CI*
Hb	-0.020	0.004	25.562	0.000	0.981	0.973-0.988
HbA1c	0.079	0.035	5.143	0.023	1.082	1.011-1.158
ABI < 0.9	0.584	0.158	13.697	0.000	1.793	1.316-2.443
TBI < 0.7	0.944	0.157	36.132	0.000	2.569	1.889-3.495
Wagner classification	1.027	0.098	109.234	0.000	2.792	2.303-3.384
PAD	0.851	0.154	30.454	0.000	2.343	1.731-3.170

3.4 Different Wagner Rates of Amputation

According to the Wagner classification of diabetic foot, the amputation rate increased significantly with the increase of the severity of a diabetic foot. Wanger grade 4-5 diabetes mellitus had a much greater amputation rate than grade 0-3 diabetic foot mellitus, whereas grade 5 diabetic foot mellitus had a 53.3 % amputation rate (Table 4).

Table 4: Comparison of the incidence of minor amputation in different Wagner grades.

Wagner grades	n	Minor amputation	minor amputation rate(%)
0	12	0	0
1	44	2	4.5
2	127	25	19.7
3	230	73	31.7
4	527	327	62.0
5	15	8	53.3

4. Discussion

Diabetic foot is one of the most common causes for diabetic people to be hospitalized, with extended hospitalization times, high costs, problematic ulcer healing, and even amputation as a last alternative. The diabetic foot is the leading cause of non-traumatic amputation[10]. Minor amputations at or below the ankle level are classified as minor amputations, whereas large amputations above the ankle level are classified as major amputations. Limb has shown a remarkable reduction in the rate of major amputations in recent years. Since minor amputation itself has no serious impact on the life and quality of DF patients, the prognosis is improved. Currently, minor amputations account for the majority of DF amputations[11]. As DF patients have higher expectation of prognosis, there are higher requirements for limb salvage, especially for relatively mild DF patients. Therefore, early identification of high risk factors for minor DF amputation is critical for severe patients to avoid major amputation and for patients with mild DF to save limbs. The indications for minor amputation are primarily because local DF limbs are difficult to maintain, whereas the indications for major amputation are primarily DF's severe and extensive disease, which is frequently accompanied by systemic infection and even life-threatening diseases. Previous studies have shown that DF healing is a complex pathophysiological process involving multiple factors, including age, patients' self-management level, daily behaviors and activities, complications of diabetes, severity of foot ulceration, nutritional status and psychology, etc [12-15].

One of the major indices used to assess the general nutritional state of diabetic foot is hemoglobin and albumin. Hemoglobin and albumin levels were statistically significant (P<0.05) between diabetic foot minor amputation and non-amputation groups in a single factor analysis. Logistic regression results of this study showed that high hemoglobin level was an independent protective factor for minor diabetic foot amputation, and the difference was statistically significant (P<0.05), and the hemoglobin and albumin levels in the minor amputation group were lower than those in the non-amputation group. Studies have shown that anemia can affect wound healing [16,17]. Related studies have reported that hypoproteinemia has been proved to be prone to wound infection and delay wound healing[18]. Another study reported an increased risk of amputation in diabetic foot patients with egg white <2.8g/dL [19]. These results suggest that hemoglobin and albumin may play a role in diabetic foot amputation. With blood transfusions and albumin supplements, we can treat anemia in diabetic foot patients and reduce the incidence of minor amputations.

In univariate analysis, our study found that the average fasting blood glucose value of the minor amputation group was greater than that of the diabetic foot without amputation group, with statistical significance (P <0.05). According to the results of this study, increasing HbA1c is a risk factor for diabetic foot minor amputation, with the mean HbA1C in the minor amputation group being greater than in the non-amputation group. Fasting blood glucose and glycosylated hemoglobin are one of the important indexes to evaluate the severity of diabetes. Poor blood sugar control in diabetic foot patients increases the risk of amputation by three times [20]. Blood glucose management is critical in the treatment of diabetic foot patients because high blood glucose levels decrease white blood cell activity, interfere with autoimmune, and worsen diabetic foot infection [21]. Control of blood glucose has been reported in some studies to reduce the risk of microvascular and neuropathic complications and progression [22]. Early control of blood glucose level is beneficial to the prevention and treatment of minor diabetic foot amputation.

DF concomitant infection is an important cause of amputation disability in DF patients [23]. In this study, the difference in WBC between the two groups was statistically significant (P <0.05), with the minor amputation group having a higher WBC count than the non-amputation group. Diabetic foot ulcers are more likely to cause infection. Diabetic foot amputees almost always have ulcers on their feet, which may lead to increased white blood cells. Research by Lin also discovered that having a greater white blood cell count increases the risk of diabetic foot amputation [24]. Active infection management may help minimize the incidence of minor amputation in diabetic foot patients when combined with strict glucose control and better overall nutritional intake.

PAD, low ABI, and low TBI were found to be independent risk factors for minor diabetic foot amputation in the current research. Peripheral arterial disease (PAD) is one of the complications of diabetes that diabetic podiatrists are most concerned about. Diabetic patients develop PAD as a result of a complicated interaction of hemodynamic, metabolic, and neurohormonal factors, resulting in endothelial dysfunction and atherosclerosis [25]. The Ankle-Brachial Index (ABI) is widely acknowledged as a simple, non-invasive test for screening PAD and assessing blood flow to the lower limbs, and it is the preferred diagnostic for screening PAD in all guidelines [26-28]. Some studies indicate that ABI and TBI are two accurate, simple and non-invasive indicators for the diagnosis of PAD, especially in DM patients with better sensitivity of TBI [29, 30].

In general, the rate of DF amputation increases with the depth of foot ulcers and the severity of Wagner's grading. Wagner grade 0-2 foot ulcers can generally heal because they do not involve bone tissue, while Wagner grade≥3 indicates that the amputation rate of infected bone tissue is much higher [23, 31]. Bruun reports that Wagner's grade 4 and above foot ulcers increase the risk of lower limb amputation by nearly six times [32]. The results of this study showed that, compared with the non-amputation group, the minor amputation group had a larger proportion of patients with Wagner grade 4-5. The severity and depth of foot ulcers are closely related to severe ischemia, infection and nutritional status of the lower extremities. Abundant blood supply and adequate camp support of lower limbs are very important for tissue repair, regeneration and anti-inflammatory effects of foot wounds. When DF patients are combined with lower limb ischemia and poor nutritional condition, local ulcers get deeper and more aggravated, leading to amputation [33]. The Wagner scale was found to be an independent risk factor for diabetic foot minor amputation in this study.

There are several limitations to this study. It is a retrospective study with inpatients rather than outpatients as the study population. The complications of DF are more serious, and the clinical characteristics of DF patients at all stages cannot be properly represented. Following that, multi-channel, multi-center, and large-sample DF patients should be included as the study population to validate prediction accuracy in clinical practice.

Conclusion

In summary, HbA1c, ABI<0.9, TBI<0.7, Wagner grading and PAD are all risk factors for diabetic minor foot amputation. Clinicians should be on the lookout for DF patients who have the aforementioned risk factors, control blood glucose at an early stage, actively increase blood circulation, and maintain efficient infection control to avoid diabetic minor foot amputation.

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Ethics Approval and Consent to Participate

This study was conducted with the approval from the Ethics Committee of Air Force Medical Center, PLA (No.2021-100-PJ01).
This study was conducted in accordance with the declaration of Helsinki.
Written informed consent was obtained from all participants.

Availability of Data and Materials

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

Competing Interests

The authors report no conflicts of interest in this work

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