



# Incidence and risk factors for poor perioperative blood glucose management in patients with diabetic foot: a retrospective study

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**Background:** Diabetic foot (DF) is one of the most serious complications of diabetes mellitus (DM). In some cases of DF, life-saving amputation is necessary. This study set out to investigate the situation of preoperative blood glucose management in patients with DF.

**Methods:** A retrospective study was performed in two centers between January 2015 and June 2018. Adult patients who received surgical treatment for DF, including amputation, debridement, and flap or skin graft, were included. Demographic and clinical data of the patients were collected. All patients were followed up for at least 3 years, until June 2021. The study outcomes included postoperative mortality, and the incidences of postoperative renal impairment, surgical infection, complete wound closure within 3 months, and reamputation. Univariable and multivariable logistic regression analyses were performed to determine the risk factors for adverse outcomes and poor blood glucose management. Kaplan-Meier curves were generated to compare survival between patients with different preoperative levels of blood glucose.

**Results:** This study included 268 patients with DF, who were divided into four groups: normal (n=72), hyperglycemia (n=95), hypoglycemia (n=44), and mixed (n=57). Total mortality was much higher in the hyperglycemia, hypoglycemia, and mixed groups than in the normal group (P=0.030, 0.009, and 0.014, respectively). The incidences of surgical infection, complete wound closure within 3 months, and reamputation were significantly higher in the hyperglycemia, hypoglycemia, and mixed groups than in the normal group. Older age and a longer duration of DM were confirmed to be important risk factors for hyperglycemia, hypoglycemia, and mixed hyperglycemia and hypoglycemia. Having higher levels of glycosylated hemoglobin (HbA1c) and creatinine and a lower level of albumin was identified as a risk factor for hyperglycemia, hypoglycemia, or mixed hyperglycemia and hypoglycemia.

**Conclusions:** This study emphasizes the importance of perioperative blood glucose management for patients with DF and provides a basis for blood glucose management of these patients in the future.

**Keywords:** Diabetic foot (DF); perioperative blood glucose; incidence; risk factors; retrospective study

Submitted Sep 28, 2021. Accepted for publication Nov 16, 2021.

doi: 10.21037/apm-21-3095

View this article at: <https://dx.doi.org/10.21037/apm-21-3095>

## Introduction

Diabetes mellitus (DM) is one of the world's most common chronic illnesses. According to World Health Organization data, in 2017, 425 million people had DM globally (1). DM can seriously endanger patients' physical and mental health. In diabetic patients, failure to control the level of blood glucose will result in hyperglycemia, which damages both large and micro blood vessels, leading to a series of complications, such as retinopathy, nephropathy, and cardiovascular complications (2-6).

Diabetic foot (DF) is one of the most serious complications of DM, and is usually accompanied by diabetic nephropathy and/or peripheral arterial disorders (7). Its main causes are peripheral nerve sensory impairment, lower extremity vascular disease, and bacterial infection. Common symptoms of DF include pain, ulcer, and gangrene of the foot (4), which can seriously damage patients' mobility and increase their psychological and economic burden. Approximately 15–25% of diabetic patients suffer from DF (8,9). Treatments for DF include debridement, infection control, and vascular reconstruction on the basis of proper control of blood glucose.

Poor management of blood glucose in patients with DF exacerbates the symptoms of foot ulcer, resulting in life-saving amputation being necessary. A DF amputation can be major or minor, which mainly depends on the size of the lesion. However, because most patients with DF have poor blood glucose management and thus have varying degrees of damage to many organs, including the liver and kidney, the postoperative survival time of patients undergo amputation for DF is much shorter than that of diabetic patients without DF (10-13). According to previous reports, the 5-year survival rate of patients with DF after amputation is only approximately 30–40% (10,13). Therefore, establishing the preoperative risk factors which affect the prognosis of patients with DF who require amputation is of great significance to improving their survival time and quality of life. However, there have been few studies on this matter to date.

Blood glucose management is known to be one of the most important factors affecting the prognosis of patients with DF. In addition to hyperglycemia, hypoglycemia in DM has gradually been recognized as a risk factor for poor prognosis. Previous research has also pointed out that hypoglycemia is an independent risk factor for any severe amputation in patients with DF (14). Therefore, we performed a retrospective two-center study to investigate

the situation of preoperative blood glucose management in patients with DF requiring surgical treatment, the impact of preoperative hyperglycemia or hypoglycemia on the prognosis of these patients, and the risk factors for poor preoperative blood glucose management. We present the following article in accordance with the STROBE reporting checklist (available at <https://dx.doi.org/10.21037/apm-21-3095>).

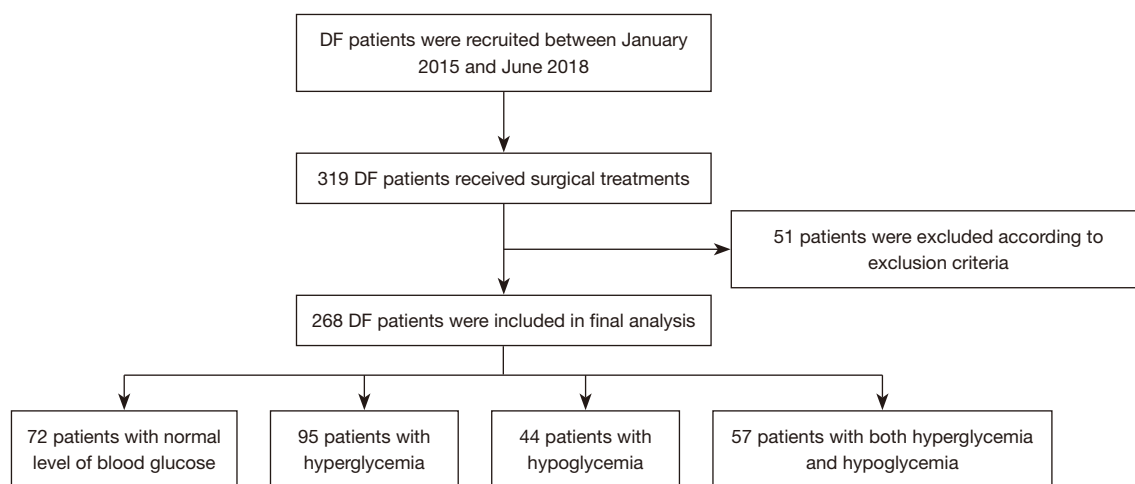
## Methods

### *Patient selection*

Patients with DF who were admitted to the First and Second Affiliated Hospitals of Soochow University between January 2015 and June 2018 were initially recruited. Only adult patients with DF who received surgical treatment, including amputation, debridement, and flap or skin graft, were included in this study. The following patients were excluded: (I) patients over 80 years of age; (II) patients undergoing surgical treatment for reasons other than DF; (III) patients with type 1 DM; (IV) patients with malignant tumors or other life-threatening diseases; and (V) patients for whom there was a severe lack of data or with incomplete follow-up.

This study was approved by the ethics committees of both the First Affiliated Hospital of Soochow University and the Second Affiliated Hospital of Suzhou University (No. 2020-033), and was conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013). Due to the study's retrospective design, it was not necessary to obtain written informed consent from the participants.

Demographic and clinical data of the study participants were collected by two investigators. These data included the following: age; sex; duration of diabetes; insulin treatment; Wagner grade; history of DF; history of amputation; the presence of osteomyelitis, retinopathy, neuropathy, peripheral vascular disease, or hypertension; smoking history; alcohol use history; preoperative newest level of blood glucose; preoperative white blood cell count; plasma C-reactive protein (CRP); glycosylated hemoglobin (HbA1c); total cholesterol; triglycerides; low-density lipoprotein (LDL) cholesterol; high-density lipoprotein (HDL) cholesterol; and albumin and creatinine. The presence of osteomyelitis was determined by imaging examination; the presence of retinopathy was determined by fundus fluorescein angiography; and neuropathy was



**Figure 1** Flow chart of patient enrollment. DF, diabetic foot.

determined on the basis of the level of urea nitrogen and/or creatinine. Hyperglycemia was defined as when at least three out of five blood glucose measurements exceeded 13.9 mmol/L preoperatively. Hypoglycemia was defined as when at least one out of three blood glucose measurements was less than 3.9 mmol/L preoperatively.

All study participants were followed up for at least 3 years, until June 2021. The primary study outcome was postoperative mortality. Secondary outcomes included the incidences of postoperative renal impairment, surgical infection, complete wound closure within 3 months, and reamputation. Postoperative renal impairment was defined as an increase in creatinine of at least two folds compared with baseline, and output of less than 0.5 mL/kg/h for more than 6 hours. Surgical infection was defined as redness, swelling, heat, and pain in the wound area and positive culture of secretion.

### Statistical analysis

Statistical analyses were performed using SPSS 20.0 (IBM Corp. NY, USA). The study participants were divided into four groups: the normal blood glucose group, a hyperglycemia group, a hypoglycemia group, and a mixed hyperglycemia and hypoglycemia group. Continuous data such as age, duration of diabetes, preoperative blood glucose level, and other markers were expressed as means with standard deviations; categorical data were expressed as numbers and percentages. Student's *t*-test was used for comparisons of continuous data between two groups, and

the chi square test was used for comparisons of categorical data between two groups. Univariable and multivariable logistic regression analyses were performed to identify the risk factors for adverse outcomes and poor blood glucose management. Kaplan-Meier curves were generated to compare survival between patients with different preoperative blood glucose levels. A *P* value of less than 0.05 was considered to indicate a significant difference.

### Results

Patients with DF who received surgical treatment at two institutions were included in this study. According to the inclusion and exclusion criteria, 268 out of 319 patients with DF were ultimately enrolled (*Figure 1*). The patients were divided into the normal ( $n=72$ ), hyperglycemia ( $n=95$ ), hypoglycemia ( $n=44$ ), and mixed ( $n=57$ ) groups.

Demographic and clinical data of the 268 included patients are exhibited in *Table 1*. The patients had a mean age of  $58.9 \pm 12.6$  years old, and 201 of them (75.0%) were male. The mean duration of DM was almost 15 years, and approximately 90% of patients were receiving insulin treatment. Half of the patients were Wagner grade 3. One hundred (37.3%) and 54 (20.1%) patients had a history of DF and amputation, respectively. Sixty-five patients (24.3%) were diagnosed with osteomyelitis. Regarding chronic comorbid diseases, 81 patients (30.2%) had retinopathy, 156 patients (58.2%) had neuropathy, 249 patients (92.9%) had peripheral vascular disease, and 123 patients (45.9%) had hypertension. Among the patients, 119 (44.4%) had a

**Table 1** Demographic and clinical data of patients with DF

Data	Total
Number	268
Age (year), mean $\pm$ SD	58.9 $\pm$ 12.6
Male sex, n (%)	201 (75.0)
Duration of DM (year), mean $\pm$ SD	14.9 $\pm$ 4.8
Insulin treatment, n (%)	242 (90.3)
Wagner grade of DF, n (%)	
3	88 (32.8)
4	133 (49.6)
5	47 (17.5)
History of DF, n (%)	100 (37.3)
History of amputation, n (%)	54 (20.1)
Osteomyelitis, n (%)	65 (24.3)
Retinopathy, n (%)	81 (30.2)
Neuropathy, n (%)	156 (58.2)
Peripheral vascular disease, n (%)	249 (92.9)
Hypertension, n (%)	123 (45.9)
History of smoking, n (%)	119 (44.4)
Alcohol use, n (%)	130 (48.5)
Blood glucose (mmol/L), mean $\pm$ SD	11.4 $\pm$ 5.8
White cell count ( $10^9/L$ ), mean $\pm$ SD	10.2 $\pm$ 3.7
CRP (mg/L), mean $\pm$ SD	9.8 $\pm$ 4.9
HbA1c (%), mean $\pm$ SD	9.5 $\pm$ 3.9
Total cholesterol (mmol/L), mean $\pm$ SD	4.2 $\pm$ 2.0
Triglycerides (mmol/L), mean $\pm$ SD	2.0 $\pm$ 1.2
LDL cholesterol (mmol/L), mean $\pm$ SD	2.4 $\pm$ 1.0
HDL cholesterol (mmol/L), mean $\pm$ SD	1.0 $\pm$ 0.3
Albumin (g/L), mean $\pm$ SD	36.2 $\pm$ 5.9
Creatinine ( $\mu\text{mol/L}$ ), mean $\pm$ SD	173.6 $\pm$ 48.4

CRP, C-reactive protein; DF, diabetic foot; DM, diabetes mellitus; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.

history of smoking and 130 (48.5%) had a history of alcohol use. The blood glucose level of the included patients was not well controlled in general, with a mean level of 11.4 $\pm$ 5.8 mmol/L. The mean HbA1c level was 9.5 $\pm$ 3.9%, and the mean creatinine level was 173.6 $\pm$ 48.4  $\mu\text{mol/L}$ , which

was significantly higher than normal level.

*Table 2* compares the demographic and clinical data of the four groups of patients. The normal group was much younger than the hyperglycemia, hypoglycemia, and mixed groups ( $P=0.001$ ,  $0.002$ , and  $0.003$ , respectively). The duration of DM was much shorter in the normal group than in the other three groups (all  $P<0.001$ ). Both the hyperglycemia and mixed groups had higher numbers of patients with diabetic neuropathy [62 (65.3%) and 37 (64.9%), respectively] than the normal group (34 patients (47.2%)). The HbA1c level was 10.0 $\pm$ 3.0% and 11.7 $\pm$ 5.7% in the hyperglycemia and mixed groups, respectively, which was higher than the level observed in the normal group (8.3 $\pm$ 2.8%). Of the four groups, the hyperglycemia group had the highest preoperative triglyceride levels (2.3 $\pm$ 1.6 mmol/L). The preoperative albumin level was significantly lower in the hypoglycemia and mixed groups than in the normal group ( $P<0.001$  and  $P=0.022$ , respectively). The hyperglycemia group had the highest preoperative creatinine levels (188.3 $\pm$ 48.2  $\mu\text{mol/L}$ ) among the four groups.

The postoperative outcomes of the study participants are summarized in *Table 3*. Patients in the hypoglycemia group had a much higher 3-year mortality rate than those in the normal group (47.7% *vs.* 26.4%). Total mortality in the hyperglycemia, hypoglycemia, and mixed groups was much higher than that in the normal group ( $P=0.030$ ,  $0.009$ , and  $0.014$ , respectively). Kaplan-Meier curves were generated to compare survival between the four groups and are shown in *Figure 2*. The results indicated that the survival rates of patients in the hyperglycemia, hypoglycemia, and mixed groups were much lower than that in the normal group ( $P=0.041$ ,  $0.002$ , and  $0.022$ , respectively). In terms of secondary outcomes, the incidences of surgical infection, complete wound closure within 3 months, and reamputation were much lower in the normal group than in the other three groups. Meanwhile, the incidence of renal impairment was similar between the four groups, showing no significant difference.

Next, multivariable logistic regression was performed to identify the predictors of several adverse outcomes, as shown in *Table 4*. Poor blood glucose management, older age, a history of amputation, neuropathy, and a high HbA1c level were confirmed to be predictors of total mortality. Furthermore, poor blood glucose management was also related to an increased incidence of other adverse outcomes. Older age, a low albumin level, osteomyelitis, a high HbA1c

**Table 2** Comparisons of demographic and clinical data of between the normal group and the other three groups

Data	Normal group	Hyperglycemia group	Hypoglycemia group	Mixed group	P1	P2	P3
Number	72	95	44	57			
Age (year), mean ± SD	53.8±13.7	60.4±11.7	61.0±10.7	61.1±13.6	0.001	0.002	0.003
Male sex, n (%)	49 (68.1)	75 (78.9)	30 (68.2)	47 (82.5)	0.111	0.989	0.063
Duration of DM (year)	11.7±4.6	17.0±4.1	14.8±4.0	15.4±4.9	<0.001	<0.001	<0.001
Insulin treatment, n (%)	63 (87.5)	82 (86.3)	42 (95.5)	55 (96.5)	0.823	0.156	0.069
Wagner grade of DF, n (%)					0.824	0.380	0.407
3	21 (29.2)	32 (33.7)	14 (31.8)	21 (36.8)			
4	38 (52.7)	47 (49.5)	18 (40.9)	30 (52.6)			
5	13 (18.1)	16 (16.8)	12 (27.3)	6 (10.5)			
History of DF, n (%)	28 (38.9)	38 (40.0)	13 (29.5)	21 (36.8)	0.884	0.307	0.812
History of amputation, n (%)	14 (19.4)	19 (20.0)	8 (18.2)	13 (22.8)	0.929	0.866	0.641
Osteomyelitis, n (%)	19 (26.4)	18 (18.9)	10 (22.7)	18 (31.6)	0.251	0.659	0.517
Retinopathy, n (%)	16 (22.2)	33 (34.7)	11 (25.0)	21 (36.8)	0.079	0.731	0.068
Neuropathy, n (%)	34 (47.2)	62 (65.3)	23 (52.3)	37 (64.9)	0.020	0.598	0.045
Peripheral vascular disease, n (%)	65 (90.3)	90 (94.7)	41 (93.2)	53 (93.0)	0.269	0.589	0.585
Hypertension, n (%)	34 (47.2)	37 (38.9)	15 (34.1)	37 (64.9)	0.145	0.165	0.045
History of smoking, n (%)	29 (40.3)	42 (44.2)	23 (52.3)	25 (43.9)	0.611	0.208	0.682
Alcohol use, n (%)	38 (52.8)	37 (38.9)	27 (61.4)	28 (49.1)	0.075	0.366	0.680
Blood glucose (mmol/L), mean ± SD	8.4±2.8	17.4±2.9	3.3±0.5	11.3±3.0	<0.001	<0.001	<0.001
White cell count (10 <sup>9</sup> /L), mean ± SD	9.7±3.9	10.6±4.0	9.5±3.0	10.5±3.5	0.148	0.730	0.233
CRP (mg/L), mean ± SD	11.5±5.2	10.3±4.6	10.8±4.7	11.0±3.9	0.224	0.256	0.487
HbA1c (%), mean ± SD	8.3±2.8	10.0±3.0	7.5±2.7	11.7±5.7	<0.001	0.172	<0.001
Total cholesterol (mmol/L), mean ± SD	4.1±1.5	4.5±2.4	4.2±1.8	3.6±1.9	0.254	0.751	0.069
Triglycerides (mmol/L), mean ± SD	1.8±0.8	2.3±1.6	1.7±0.9	2.0±0.9	0.025	0.617	0.157
LDL cholesterol (mmol/L), mean ± SD	2.4±0.9	2.6±1.0	2.0±1.0	2.4±1.1	0.163	0.049	0.857
HDL cholesterol (mmol/L), mean ± SD	1.0±0.3	1.0±0.3	1.1±0.3	1.1±0.3	0.137	0.332	0.433
Albumin (g/L), mean ± SD	37.4±5.8	37.4±5.4	32.4±3.8	34.7±6.7	0.990	<0.001	0.022
Creatinine (μmol/L), mean ± SD	161.8±37.2	188.3±48.2	162.2±44.1	172.9±58.1	<0.001	0.960	0.192

P1: normal group vs. hyperglycemia group; P2: normal group vs. hypoglycemia group; P3: normal group vs. mixed group. DM, diabetes mellitus; CRP, C-reactive protein; DF, diabetic foot; DM, diabetes mellitus; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.

level, a history of amputation, and a history of smoking were identified as predictors of one or two adverse outcomes.

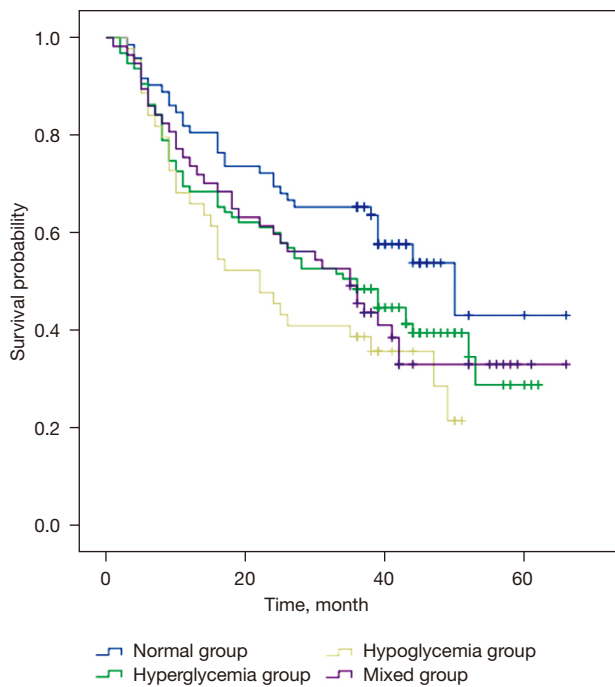
Finally, the risk factors for poor blood glucose management were determined (*Table 5*). After adjusting for the variables identified through univariable logistic

regression, older age and a longer duration of DM were confirmed as important risk factors for hyperglycemia, hypoglycemia, and mixed hyperglycemia and hypoglycemia. High levels of HbA1c and creatinine were identified to be risk factors for hyperglycemia; a low albumin level was

**Table 3** Outcomes of patients with DF after receiving surgical treatment

Data	Normal group, n (%)	Hyperglycemia group, n (%)	Hypoglycemia group, n (%)	Mixed group, n (%)	P1	P2	P3
Number	72	95	44	57	–	–	–
Three-year mortality	19 (26.4)	35 (36.8)	21 (47.7)	20 (35.1)	0.153	0.019	0.285
Total mortality	31 (43.1)	57 (60.0)	30 (68.2)	37 (64.9)	0.030	0.009	0.014
Renal impairment	36 (50.0)	52 (54.7)	19 (43.2)	25 (43.9)	0.544	0.475	0.488
Surgical infection	4 (5.6)	16 (16.8)	10 (22.7)	13 (22.8)	0.026	0.006	0.004
Complete wound closure	63 (87.5)	69 (72.6)	28 (63.6)	32 (56.1)	0.019	0.002	<0.001
Reamputation	12 (16.7)	29 (30.5)	17 (38.6)	20 (35.1)	0.039	0.008	0.016

DF, diabetic foot.

**Figure 2** Kaplan-Meier curves of the four groups of patients.

identified as a risk factor for hypoglycemia; and high HbA1c and low albumin levels were identified as risk factors for mixed hyperglycemia and hypoglycemia.

## Discussion

Very few studies to date have explored the effects of poor blood glucose management in patients with DF undergoing surgical treatment. As far as we know, this is the first study to investigate the current situation of perioperative blood

glucose management in patients with DF. The results of our study indicate that poor blood glucose management is extremely common in patients with DF, affecting up to 73.1% of them, and most commonly leads to hyperglycemia. Poor blood glucose management significantly impacts patients' postoperative prognosis, considerably reducing their postoperative survival and increasing the occurrence of adverse outcomes such as surgical infection, incomplete wound closure, and reamputation. The most important risk factors for poor blood glucose management include older age and longer duration of DM; other risk factors, such as high levels of creatinine and albumin, may also play a role to some extent.

Many previous studies have focused on the risk factors for amputation in patients with DF (8,11,15-17), and few studies have investigated the preoperative blood glucose management of patients who require surgical treatment for DF. The results of the present study revealed that most patients had poor blood glucose management before surgery, which is consistent with observations in previous reports (18-20). The most common blood glucose-related condition in our patients was hyperglycemia. Perioperative hyperglycemia has been proved by many studies to be related to postoperative surgical infection, poor wound healing, and other prognostic outcomes (21-23). The cause of death in patients with DF during the perioperative period was the combination of different adverse outcomes induced by poor management of blood glucose. The results of our study also found that hyperglycemia may be related to the incidence of reamputation. According to risk factor analysis, older age, a long duration of DM, and renal impairment were the most important risk factors for preoperative hyperglycemia. This result can be explained



**Table 4** Predictors of adverse postoperative outcomes in patients with DF

Data	P value	Odds ratio	95% confidence interval
<b>Total mortality</b>			
Blood glucose management			
Normal	Reference		
Hyperglycemia	0.018	2.158	1.143–4.073
Hypoglycemia	0.012	2.759	1.249–6.097
Mixed	0.020	2.360	1.144–4.866
Older age	0.026	1.016	1.003–1.030
History of amputation	0.012	1.722	1.161–2.752
Neuropathy	0.036	1.555	1.036–2.427
High HbA1c level	0.003	1.481	1.141–1.923
<b>Surgical infection</b>			
Blood glucose management			
Normal	Reference		
Hyperglycemia	0.043	3.305	1.039–10.513
Hypoglycemia	0.003	7.330	1.996–26.915
Mixed	0.011	5.044	1.457–17.461
Older age	0.036	1.069	1.011–1.124
Low albumin level	0.043	1.088	1.008–1.175
<b>Incomplete wound closure</b>			
Blood glucose management			
Normal	Reference		
Hyperglycemia	0.005	3.861	1.520–9.803
Hypoglycemia	<0.001	5.495	2.294–13.889
Mixed	0.020	2.695	1.167–6.211
Older age	0.024	1.063	1.013–1.136
Osteomyelitis	0.004	1.936	1.134–3.313
High HbA1c level	0.027	1.192	1.039–1.372
Low albumin level	0.041	1.302	1.015–1.681
<b>Reamputation</b>			
Blood glucose management			
Normal	Reference		
Hyperglycemia	0.048	2.157	1.007–4.621
Hypoglycemia	0.009	3.190	1.337–7.613

**Table 4** (continued)**Table 4** (continued)

Data	P value	Odds ratio	95% confidence interval
Mixed	0.018	2.701	1.183–6.169
History of amputation	0.020	1.941	1.110–3.395
History of smoking	0.026	2.299	1.096–4.822
High HbA1c level	0.004	1.088	1.027–1.153

DF, diabetic foot; HbA1c, glycosylated hemoglobin.

**Table 5** Risk factors for poor blood glucose management in postoperative patients with DF

Data	P value	Odds ratio	95% confidence interval
<b>Hyperglycemia</b>			
Older age	0.002	1.058	1.020–1.097
Longer duration of DM	<0.001	1.354	1.209–1.517
Neuropathy	0.094	2.113	0.881–5.066
High HbA1c level	<0.001	1.372	1.160–1.622
High creatinine level	<0.001	1.020	1.009–1.031
<b>Hypoglycemia</b>			
Older age	0.049	1.042	1.000–1.087
Longer duration of DM	0.001	1.198	1.074–1.337
Low albumin level	<0.001	1.229	1.110–1.359
<b>Mixed</b>			
Older age	0.004	1.053	1.017–1.091
Longer duration of DM	<0.001	1.200	1.086–1.327
High HbA1c level	<0.001	1.255	1.119–1.407
Low albumin level	0.184	1.047	0.978–1.121

DF, diabetic foot; DM, diabetes mellitus; HbA1c, glycosylated hemoglobin.

by decreased compliance in elderly patients after long-term treatment, which aggravates peripheral vascular disease and hyperglycemia. Therefore, effective management of hyperglycemia is crucial for the postoperative prognosis of patients with DF, and hyperglycemia should be corrected and stabilized before surgery.

In recent years, increasing attention has been paid to the role of hypoglycemia in DF. Studies have pointed out that hypoglycemia may be more dangerous to patients

with DF than hyperglycemia, and may lead to a significant increase in the amputation rate and mortality (24-28); these findings are reinforced by the results of the present study. Postoperative mortality was significantly higher in hypoglycemic DF patients than in patients in the other three groups. According to previous studies, there are many risk factors for hypoglycemia, including old age, chronic liver disease, heart failure, a long duration of DM, malnutrition, and renal insufficiency. In this study, multivariable logistic regression analysis of risk factors for hypoglycemia showed that old age, a long duration of DM, and a low level of albumin were important factors for the occurrence of hypoglycemia, which was consistent with previous results. Our initial hypothesis was that the dose and frequency of insulin use may also play a key role in patients with DF; however, as a retrospective study, it was difficult for us to obtain the complete medication information of patients, and so the impact of insulin use on blood glucose management is still unclear.

Initially, we also proposed the hypothesis that patients with mixed hyperglycemia and hypoglycemia before surgery may have the worst prognosis of all, as such patients have the poorest blood glucose management, and their normal organ function may be severely challenged. However, our results revealed no significant prognostic difference between patients with mixed hyperglycemia and hypoglycemia and those with simple hyperglycemia or hypoglycemia. This result may be explained by the small sample size of this study; increasing sample size in future may give us a deeper understanding of this problem. The occurrence of hyperglycemia indicates that the patient may have poor blood glucose control due to insufficient drug dose or frequency, or excessive carbohydrate consumption, whereas the occurrence of hypoglycemia indicates that the patient may have excessive drug dose or insufficient carbohydrate consumption. This contradiction reveals a current dilemma of diabetes: how to find a balance to best control blood glucose levels. Therefore, the preoperative occurrence of mixed hyperglycemia and hypoglycemia in patients with DF is worthy of discussion.

There were some limitations in this study. First, the study participants were divided into four groups for analysis, and the number of patients in each group was not large enough to investigate more risk factors for poor blood glucose management. This may have led to some deviation in the study results. Second, detailed data of insulin use could not be collected due to the study's retrospective nature. The insulin dose and frequency may have been one

of the main risk factors causing poor preoperative blood glucose management in the patients in this study. However, we could only obtain data on whether or not insulin was being used, which is the aspect of this study that requires the most improvement. Thirdly, the duration of follow-up in this study was shorter than that in previous studies, and the long-term prognosis of our patients is still unclear.

To conclude, this study has illuminated the situation of perioperative blood glucose management in patients with DF from two centers and has identified some risk factors for poor blood glucose management. The results of this study reemphasize the importance of effective blood glucose management in patients with DF, and provide a basis for blood glucose management of such patients in the future.

### Acknowledgments

*Funding:* None.

### Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://dx.doi.org/10.21037/apm-21-3095>

*Data Sharing Statement:* Available at <https://dx.doi.org/10.21037/apm-21-3095>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://dx.doi.org/10.21037/apm-21-3095>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the ethics committees of both the First Affiliated Hospital of Soochow University and the Second Affiliated Hospital of Suzhou University (No. 2020-033), and was conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013). Due to the study's retrospective design, it was not necessary to obtain written informed consent from the participants.

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- (English Language Editor: J. Reylonds)

**Cite this article as:** Chen X, Wu M, Hu Q, Cheng X. Incidence and risk factors for poor perioperative blood glucose management in patients with diabetic foot: a retrospective study. *Ann Palliat Med* 2021;10(12):12300-12309. doi: 10.21037/apm-21-3095