

# Clinical Characteristics of Inpatients with Diabetic Foot Ulcer Admitted with Non-Ulcer Complaints: A Retrospective Study

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**Background:** Diabetic foot ulcer (DFU) inpatients admitted with non-ulcer complaints constitute a neglected group that might suffer from more non-standard treatments. This study intends to describe their clinical characteristics, and clarify the problems existing in the DFU management process.

**Methods:** In this retrospective study, admission complaints were determined by combining the final diagnosis and clinical documentation, and were categorized as: ulcer-related or non-ulcer complaints.

**Results:** A total of 264 DFU inpatients were included in the final analysis, of which, 80 (30.3%) were admitted with non-ulcer complaints. A total of 82.5% of the DFU inpatients with non-ulcer complaints were admitted to departments without DF specialists. IWGDF/IDSA grade, cerebrovascular diseases, chronic kidney disease, infection in other parts, glycosylated hemoglobin A1c and the source of hospitalization expenses were the independent influencing factors for admission with non-ulcer complaints (all  $P < 0.05$ ). Before admission, only 11.3% of the patients with non-ulcer complaints had ever been treated by a DF specialist and/or in a clinical setting with DF specialists. After admission, 25.0% of the DFU inpatients with non-ulcer complaints did not receive any local wound care, and only 7.6% of the patients admitted to the departments without DF specialists obtained a referral.

**Conclusion:** Approximately one-third of inpatients with DFU are admitted with non-ulcer complaints and most of them are admitted to departments without DF specialists. Inpatients with non-ulcer complaints have milder wounds but more severe and greater comorbidities and worse organ function. These patients do not receive standardized management for DFU either before or after admission. Targeted measures are needed to improve this situation.

**Keywords:** diabetic foot ulcer, admission complaint, non-ulcer, non-specialist

## Introduction

Standardized management for diabetic foot (DF) patients, including timely visits, reasonable referrals and professional treatment is very important, while improper management leads to a poor prognosis.<sup>1-4</sup> For a long time, specialists in this field have been committed to exploring clinical pathways for the management of DF, but there are still no widely unified strategies, and some are impracticable. Patients with DF disorders typically have other diabetic complications and comorbidities that affect their functional status, surgical risk and quality of life. Furthermore, these comorbidities are often concurrent with additional risk factors, including acute exacerbation of diseases, as well as hospitalization.<sup>5,6</sup> This makes the management of DF more complicated and difficult to standardize. At present, studies on DF have focused mainly on patients with ulcer-related complaints, whereas studies on those seeking inpatient care for non-ulcer reasons are limited.<sup>7</sup> This is a neglected but relatively large group, which might suffer from more non-standard treatments for DF. This study intends to describe the clinical characteristics of inpatients with diabetic foot ulcer (DFU) who complain of

non-ulcer disorders, clarify the problems existing in the management process, explore the corresponding solutions and provide some basis for driving quality improvement.

## Materials and Methods

### Study Design and Patients

This study was retrospective and observational. The subjects were DF inpatients who were admitted to the Chengdu Second People's Hospital from August 1, 2020, to January 31, 2023. In strict accordance with the principles of the International Classification of Disease tenth revision (ICD-10), data of the inpatients whose final diagnosis contained codes for "DF" or, complementarily, whose handwritten diagnosis included both "diabetes" and "ulcer", or both "diabetes" and "wound", or both "diabetes" and "gangrene", or both "diabetes" and "osteomyelitis", were retrieved and counted. Inpatients with DF were included, regardless of admitting complaints. The exclusion criteria were as follows: (1) DF in Wagner grade 0 (no existing foot ulcers); and (2) missing important data, such as insufficient evidence for the diagnosis of peripheral arterial disease (PAD) and diabetic peripheral neuropathy (DPN), and incomplete descriptions of the wounds. Admission complaints were determined by combining the final diagnosis and clinical documentation in the medical records and were categorized as: ulcer-related or non-ulcer complaints. Those with multiple admissions were grouped according to the complaints for their first admission to our hospital during the study period. The Medical Ethical Review Board of the Second People's Hospital of Chengdu approved this study (Approval No. 2023385) and the need for written informed consent was waived by this Medical Ethical Review Board of our institute due to retrospective nature of the study. The reporting of this study conformed to the STROBE statement.

### Data Collection

#### Demographic and Clinical Data During Hospitalization

The data were collected by three DF specialists. A structured questionnaire was designed and constructed in sections and included the following information: demographic profiles, medical history, physical examination, laboratory indicators, auxiliary examination, treatment before and after admission, final diagnosis and other relevant information. The demographic profiles included gender, age, marital status, habitual residence (urban or rural), and source of hospitalization expenses. Medical history included chief complaints, duration of diabetes, time interval between ulcer discovery by the patient and admission to our hospital, and long-term ( $\geq 30$  days) bedridden and smoking (continuous smoking for more than 1 year) status. Physical examination mainly referred to blood pressure (BP) and the specific assessment of the lower extremities. Blood pressure was recorded according to the values at admission. Examination of the lower extremities included location, depth, size and appearance of the wounds, and evaluation of vascular disease and neuropathy of the lower extremities. The laboratory indices were mainly the results of the first examination after admission and included fasting blood glucose (FBG), glycosylated hemoglobin A1c (HbA1c), urea, creatinine (Crea), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), triglyceride (TG), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), hemoglobin (Hb), white blood cell (WBC), procalcitonin (PCT) and hypersensitive C reactive protein (hsCRP) levels. Auxiliary examinations (if any) included the ankle-brachial index (ABI), foot X-ray, electromyography and vascular color Doppler ultrasound. The in-hospital treatment of DFU was recorded, including local care for wounds, revascularization, amputation, and other symptomatic and supportive treatments. Clinical outcomes at discharge were evaluated and classified as follows: complete healing of the wound, effective healing of the wound, ineffective healing of the wound, major amputation and death during hospitalization. Wound healing was evaluated by the percentage reduction in the wound area (RWA%), that is,  $(\text{original wound area} - \text{unhealed wound area}) / \text{original wound area} \times 100\%$ . "RWA% = 100%" was defined as complete healing (it was not needed to maintain the complete epithelization state for at least 2 weeks in this retrospective study), "RWA%  $\leq 0\%$ " was defined as ineffective healing (the wound area remained unchanged or increased), and " $0\% < \text{RWA\%} < 100\%$ " was defined as effective healing (the wound area was reduced but not to zero). Major amputation was identified as amputation above the ankle level.

The patients who complained of non-ulcer reasons were further recorded about their before-admission medical treatments, including whether to seek medical help, whether to obtain medical help from DF specialists or in clinical settings with DF specialists (if the exact specialty of medical staff was not provided), and the diagnosis and treatment measures, as well as their post-admission treatments, including whether to receive a consultation of DF specialists and whether to obtain a referral to the departments with DF specialists for DFU reasons. Our hospital had multidisciplinary input for DF care, and the DF specialists were from the departments of endocrinology, orthopedics, vascular surgery and burn and plastic surgery. The time interval between ulcer discovery by the patient and the first visit to a clinical setting was recorded for the assessment of patient delay, and the time interval between the first consultation of the non-specialists for DFU and the first consultation of the DF specialists was evaluated for professional delay. Patient delay plus professional delay was defined as diagnosis and treatment delay.

### Follow-up Data

From April 1, 2023, to May 10, 2023, all discharged patients were followed up by telephone or outpatient visits. The follow-up included readmission and death, and specifically asked about the time from the first discharge to the date of death and to the date of the first readmission, as well as the causes of readmission (ulcer-related or non-ulcer) and total number of readmissions.

## Diagnosis and Definitions

Diabetic complications and comorbidities were defined according to the final diagnosis and clinical documentation in the medical records.

### DF and Other Complications

The diagnosis of DF conformed to the definition of the International Working Group on DF (IWGDF) in 1999.<sup>8</sup> DFUs were graded according to the Wagner system and further evaluated for their infection severity on the basis of IWGDF/ Infectious Diseases Society of America (IDSA) system.<sup>9,10</sup> The PAD and DPN patients were diagnosed according to the international guidelines.<sup>11–13</sup>

### Comorbidities

Hypertension met the diagnostic criteria of the 2018 Chinese guidelines for the management of hypertension.<sup>14</sup> The diagnosis of dyslipidemia was based on the 2016 Chinese guidelines for the management of dyslipidemia in adults.<sup>15</sup> Cardiovascular diseases included coronary artery disease (CAD), valvular heart disease, cardiomyopathy, arrhythmia and external defibrillation. In addition, cardiac insufficiency was also considered. The diagnosis of heart failure referred to the 2018 Chinese guidelines for the management of heart failure.<sup>16</sup> Cerebrovascular diseases included stroke, cerebral thrombosis, transient ischemic attack, cerebral arterial stenosis, and cerebral artery occlusion. Definitions of chronic kidney disease (CKD) referred to the standard of Kidney Disease: Improving Global Outcomes (KDIGO).<sup>17</sup>

### Causes of Complaints of Inpatients with Non-Ulcer Complaints

The causes of complaints were divided into five categories: (1) Acute cardiovascular and cerebrovascular diseases: acute or serious cases of cardiovascular and cerebrovascular diseases mentioned above. (2) Related causes of renal insufficiency (RI): acute kidney injury (AKI) on CKD (A/C), progressive renal disease (PRD), new RI, complications of CKD (renal anemia, renal osteopathy, renal hypertension, uremic encephalopathy, internal environment imbalance, etc), dialysis-related problems, and related symptoms caused by RI. (3) Unbalanced diabetes: hypoglycemia, hyperglycemia and glucose variability, diabetic ketoacidosis (DKA), and hyperosmolar hyperglycemia syndrome (HHS). (4) Infections: infection of parts other than the foot ulcer, including the respiratory system, digestive system, genitourinary system, other parts of the skin and sepsis. (5) Others.

## Data Analysis and Statistics

SPSS 17.0 was used for statistical analysis. Continuous data with a non-normal distribution are expressed as the median and interquartile range (IQR), and the Wilcoxon rank-sum test was used for comparisons between groups. Categorical

data are presented as frequencies and percentages, and the  $\chi^2$  test was used for comparisons between groups. Stepwise logistic regression models that included significantly associated variables in univariate analyses were used to determine the factors affecting admission with non-ulcer complaints. Kaplan-Meier analysis was used to draw construct survival curves and calculate the mortality and readmission rates, and the Log rank test was used for comparisons between groups.  $P < 0.05$  was considered statistically significant.

## Results

### Clinical Characteristics of Inpatients with DFU

A total of 844 admission entries were retrieved, and 264 eligible cases were included in the final analysis. In the follow-up study, 29 patients fell off for various reasons. A patient flow-chart is depicted in [Supplementary Figure 1](#).

Among the inpatients with DFU, a total of 80 (30.3%) were admitted for non-ulcer complaints, and only 17.5% of the DFU inpatients with non-ulcer complaints were admitted to the departments with DF specialists. The Wagner grade and IWGDF/IDSA grade were lower (both  $P < 0.05$ ). The proportion of patients with non-ulcer complaints who stayed long-term bedridden was greater ( $P = 0.018$ ), and they were more likely to have cardiovascular diseases, heart failure, cerebrovascular diseases, CKD, dialysis, infection in other parts of the body, gastrointestinal bleeding and anemia (all  $P < 0.05$ ) (see [Table 1](#) for details). The levels of hsCRP and PCT were greater (both  $P < 0.05$ ), and the HbA1c level was lower ( $P = 0.003$ ) in those with non-ulcer complaints (see [Table 2](#) for details). Because of the differences in admission departments, not all the inpatients were measured with the relevant laboratory indicators, and the number of patients measured by each indicator is detailed in [Table 2](#).

**Table 1** Demographic and Clinical Characteristics of Inpatients with DFU

	Percentage or Median			P
	Total (N = 264)	Ulcer-Related (N = 184)	Non-Ulcer (N = 80)	
Admission department				<0.001
Endocrinology	53.0	69.6	15.0	
Orthopedics, vascular surgery or burn and plastic surgery	7.2	9.2	2.5	
Nephrology, cardiology, neurology or general practice	27.3	17.4	50.0	
Others	12.5	3.8	32.5	
Admission department with DF specialists	60.2	78.8	17.5	<0.001
Male sex	64.0	62.5	67.5	0.487
Marital status				0.040
Married	81.1	77.7	88.8	
Unmarried, widowed or divorced	18.9	22.3	11.3	
Habitual residence				0.125
Urban	63.6	66.8	56.3	
Rural	36.4	33.2	43.7	
Source of hospitalization expenses				0.033
Employee basic medical insurance	63.3	65.2	58.8	
Residents basic medical insurance	22.0	24.5	16.2	
Others	14.7	11.3	25.0	
Age (years)	70(61, 78)	69(59, 77)	72(63, 79)	0.349
Long-term bedridden status	16.3	12.5	25	0.018
Smoking status	57.6	56.0	61.3	0.498
Duration of diabetes (years)	10(3, 20)	10(3, 17)	11(7, 20)	0.122

(Continued)

**Table 1** (Continued).

	Percentage or Median			P
	Total (N = 264)	Ulcer-Related (N = 184)	Non-Ulcer (N = 80)	
Time interval between ulcer discovery by the patient and admission to our hospital (weeks)	3(1, 9)	3(2, 5)	12(2, 25) <sup>a</sup>	0.000
Wagner grade				0.001
1	14.4	10.3	23.8	
2	40.5	38.0	46.3	
3	28.0	33.2	16.3	
4	17.0	18.5	13.8	
IWGDF/IDSA grade				0.005
1 (Uninfected)	14.4	10.3	23.8	
2 (Mild)	37.1	37.0	37.5	
3 (Moderate)	42.8	45.7	36.3	
4 (Severe)	5.7	7.1	2.5	
PAD	56.4	57.1	55.0	0.788
DPN	82.2	83.2	80.0	0.600
Cardiovascular diseases	40.9	33.2	58.8	<0.001
Heart failure	25.8	20.7	37.5	0.006
Cerebrovascular diseases	24.6	18.5	38.8	0.001
CKD				<0.001
0	54.9	63.0	36.3	
1	1.9	1.6	2.5	
2	4.5	3.3	7.5	
3	14.8	17.9	7.5	
4	6.8	4.9	11.3	
5	17.0	9.2	35.0	
Dialysis	8.7	3.8	20.0	<0.001
Infection of parts other than foot ulcer	26.1	15.8	50.0	<0.001
Gastrointestinal bleeding	4.5	1.1	12.5	<0.001
Anemia	36.4	28.8	53.7	<0.001
Hypoproteinemia	37.5	34.8	43.8	0.170
Hypertension	58.0	54.3	66.3	0.079
Dyslipidemia	34.1	36.4	28.8	0.260
Malignant tumour	4.5	5.4	2.5	0.357

**Notes:** <sup>a</sup>: N = 62. For 18 patients with non-ulcer complaints were unable to determine the exact period when their ulcer started. Percentage values were rounded to one decimal place.

**Abbreviations:** CKD, chronic kidney disease; DFU, diabetic foot ulcer; DPN, diabetic peripheral neuropathy; IWGDF, International Working Group on Diabetic Foot; IDSA, Infectious Diseases Society of America; PAD, diabetic peripheral arterial disease.

**Table 2** Physical Examination and Laboratory Indicators of Inpatients with DFU

	Total		Ulcer-Related		Non-Ulcer		P
	N	Median	N	Median	N	Median	
SP (mmHg)	264	130(118, 148)	184	131(121, 147)	80	128(117, 152)	0.952
DP (mmHg)	264	72(65, 83)	184	73(65, 83)	80	69(63, 84)	0.271
WBC (10 <sup>9</sup> /L)	264	7.3(5.2, 10.8)	184	7.2 (5.4, 11.0)	80	7.4(4.7, 10.1)	0.326
Hb (g/L)	264	120(98, 133)	184	122(104.5, 133)	80	111.5 (90.5, 132)	0.072
ALB (g/L)	262	37(31, 40)	183	37(32, 41)	79	36(31, 39)	0.103
AST (U/L)	262	22(17, 30)	183	23(18, 30)	79	20 (17, 32)	0.426

(Continued)

**Table 2** (Continued).

	Total		Ulcer-Related		Non-Ulcer		P
	N	Median	N	Median	N	Median	
ALT (U/L)	262	20(12, 29)	183	21 (13, 29)	79	18 (12, 30)	0.470
Crea (umol/L)	259	89(64, 149)	179	79(62, 119)	80	118.5(70, 299)	<0.001
Urea (mmol/L)	259	8.3(5.5, 13.4)	179	8.1(5.4, 12.0)	80	8.6(5.8, 15.9)	0.065
FBG (mmol/L)	238	10.2(7.2, 14.0)	161	10.4(7.3, 14.1)	77	9.6 (6.9, 13.5)	0.274
HbA1c (%)	228	8.9(7.2, 10.7)	151	9.1(7.6, 11.0)	77	8.1 (6.6, 9.8)	0.003
TC (mmol/L)	243	4.0(3.4, 4.8)	169	4.2(3.4, 4.8)	74	3.8(3.2, 4.5)	0.035
TG (mmol/L)	243	1.4(0.9, 1.8)	169	1.3(0.9, 1.8)	74	1.6(1.0, 2.0)	0.010
LDL-C (mmol/L)	243	2.3(1.7, 2.9)	169	2.3(1.7, 2.9)	74	2.0(1.7, 2.4)	0.025
HDL-C (mmol/L)	243	1.0(0.8, 1.3)	169	1.1(0.8, 1.3)	74	0.9(0.8, 1.2)	0.008
hsCRP (mg/L)	250	8.4(0.6, 32.9)	173	8.1(0.6, 33.0)	77	15.0(0.8, 31.1)	0.044
PCT (ng/mL)	244	0.1(0.0, 0.4)	171	0.1(0.0, 0.2)	73	0.3(0.1, 1.1)	<0.001

**Notes:** Median values of WBC, urea, FBG, HbA1c, TC, TG, LDL-C, HDL-C, hsCRP, and PCT were rounded to one decimal place.

**Abbreviations:** SP, systolic pressure; DP, diastolic pressure; FBG, fasting blood glucose; HbA1c, glycosylated hemoglobin A1c; Crea, creatinine; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; TG, triglyceride; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Hb, hemoglobin; WBC, white blood cell; PCT, procalcitonin; hsCRP, hypersensitive C reactive protein.

## Factors Influencing the Admission of DFU Inpatients with Non-Ulcer Complaints

According to the final diagnosis and clinical documentation, unbalanced diabetes was the most common cause of admission complaints, followed by acute cardiovascular and cerebrovascular diseases (see [Table 3](#) for details). The results of stepwise regression analysis showed that IWGDF/IDSA grade, cerebrovascular diseases, CKD, infection in other parts, HbA1c and the source of hospitalization expenses were the independent influencing factors for admission (all  $P < 0.05$ ) (see [Table 4](#) for details).

## Diagnosis and Treatment of the Patients with Non-Ulcer Complaints Before and After Admission

Up to 81.4% of the patients had never sought medical help before admission. At admission, only 8.8% were being treated by the DF specialists and/or in the clinical settings with DF specialists. After admission, 75.0% of the patients received local wound care, and 12.5% received symptomatic analgesic treatment. A total of 86.4% of the patients admitted to the departments without DF specialists had a consultation with DF specialists, but only 7.6% obtained a referral ([Table 5](#)).

**Table 3** Causes of Admission Complaints of DFU Inpatients with Non-Ulcer Complaints

Causes of Admission Complaints	N	Percentage
Unbalanced diabetes	18	22.5
Hyperglycemia and glucose variability, DKA, and HHS	12	15.0
Hypoglycemia	6	7.5
Acute cardiovascular and cerebrovascular diseases	17	21.3
Related causes of RI	10	12.5
Infection of parts other than foot ulcer	10	12.5
Others	25	31.3

**Note:** Percentage values were rounded to one decimal place.

**Abbreviations:** DKA, diabetic ketoacidosis; HHS, hyperosmolar hyperglycemia syndrome; RI, renal insufficiency.

**Table 4** Factors Influencing Admission of DFU Inpatients with Non-Ulcer Complaints

	B	SE	Wals	Exp(B) (CI95%)	P
Infection of parts other than foot ulcer	1.307	0.359	13.275	3.696(1.829,7.471)	<0.001
IWGD/IDSA grade	-0.767	0.221	12.001	0.465(0.301,0.717)	0.001
CKD	0.243	0.082	8.690	1.274(1.085,1.498)	0.003
Source of hospitalization expenses	0.466	0.224	4.330	1.594(1.027,2.474)	0.037
Cerebrovascular diseases	0.977	0.371	6.955	3.696(1.829,7.471)	0.008
HbA1c	-0.136	0.059	5.330	0.873(0.777,0.980)	0.021
Constant	0.495	0.818	0.366	1.641	0.545

**Notes:** Source of hospitalization expenses, long-term bedridden status, IWGD/IDSA grade, cardiovascular diseases, cerebrovascular diseases, CKD, infection in other parts, and HbA1c were included in the stepwise regression analysis. Percentage values were rounded to one decimal place.

**Table 5** Diagnosis and Treatment of the DFU Inpatients with Non-Ulcer Complaints Before and After Admission

	N	Percentage
Diagnosis and treatment before admission		
Had never sought medical help	65	81.4
Had ever been treated by a DF specialist and/or in a clinical setting with DF specialists	9	11.3
Diagnosis and treatment at admission		
No treatment	46	57.5
Being treated by patients themselves	20	25.0
Being treated by the non-specialists for DF	7	8.8
Being treated by the DF specialists and/or in the clinical settings with DF specialists	7	8.8
Diagnosis and treatment after admission		
Had a consultation of DF specialists	57	86.4 <sup>a</sup>
Obtained a referral to a department with DF specialists	5	7.6 <sup>b</sup>
Received symptomatic analgesic treatment	10	12.5
Received local wound care	60	75.0

**Notes:** <sup>a</sup>: The ratio of those who had a consultation of DF specialists to the patients admitted to departments without DF specialists. <sup>b</sup>: The ratio of those who received a referral to a department with DF specialists to the patients admitted to the departments without DF specialists. Percentage values were rounded to one decimal place.

## Comparison of Clinical Outcomes Between DFU Inpatients with Ulcer-Related and Non-Ulcer Complaints

There was no significant difference in clinical outcomes between the two groups during hospitalization ( $P = 0.216$ ). A total of 28.8% of the inpatients with non-ulcer complaints were ineffectively healed, and 5% died in the hospital (Table 6). In the follow-up study, the median follow-up time was 16 (11, 24) months. No significant difference was observed in either the out-of-hospital cumulative mortality rates ( $P = 0.571$ ) or readmission rates ( $P = 0.153$ ) (Table 6). However, patients with non-ulcer complaints suffered from more readmissions ( $P = 0.012$ ) (Table 6). The Log rank test showed that there was no significant difference in either readmission rates or mortality rates between the two groups (both  $P > 0.05$ ) (Supplementary Figure 2).



**Table 6** Comparison of Clinical Outcomes Between DFU Inpatients with Ulcer-Related and Non-Ulcer Complaints

	Percentage or Median		P
	Ulcer-Related	Non-Ulcer	
Outcomes during the first hospitalization (N=264)			0.216
Complete healing	3.3	5.0	
Effective healing	72.8	61.3	
Ineffective healing	18.5	28.8	
Major amputation	4.3	0.0	
Death	1.1	5.0	
Outcomes during long-term follow-up (N=229)			
Rate of readmission	50.9	61.4	0.153
Number of readmissions	1(0, 1)	1(1, 2)	0.012
Ratio of readmission caused by DFU <sup>a</sup>	48.2	23.3	0.007
Rate of mortality	16.4	20.0	0.571

**Notes:** <sup>a</sup> The ratio of those with at least one readmission due to DFU to all the readmitted patients. Percentage values were rounded to one decimal place.

## Discussion

This study revealed that approximately one-third of inpatients with DFU were admitted with non-ulcer complaints, and most of them were admitted to departments without DF specialists. Inpatients with non-ulcer complaints had milder wounds but more severe and greater comorbidities and worse organ function. These patients did not receive standardized management for DFU either before or after admission. Previously, the clinical evidence on DFU inpatients admitted with non-ulcer complaints was limited. In this work, we provide some reference for exploring the problems in the management process.

In China, there is no agreement on the specific hospitals and departments for DF inpatients, and the most common department for DF is endocrinology in this study. There are very few occupational podiatrists in China, and the diagnosis and treatment of DF mostly depend on trained staff in the relevant clinical departments.<sup>18</sup> The endocrinologists in tertiary hospitals have greater accessibility and usually serve as the initial clinicians as well as transportation platforms. The common admission departments of DFU inpatients with non-ulcer complaints are non-endocrinology internal medicine departments, including nephrology, cardiology, neurology and general practice, thus these departments are the focus of training and improvement. In addition, DFU, when complicated with systemic infection, cardiovascular or cerebrovascular diseases, and RI were the main sources of admission with non-ulcer complaints. We should pay more attention to this population, educate them and provide appropriate guidance and suggestions. Nevertheless, it is worth mentioning that HbA1c was negatively correlated with non-ulcer complaint admission. This result might be related to more anemia and lower Hb levels (although the difference was not statistically significant) in non-ulcer complaint patients and, more importantly, more interventions for cardiovascular risk factors, such as blood glucose and lipids (TC and LDL-C were significantly lower in these patients, Table 2). The relatively high incidence of hypoglycemia (one-third of those with unbalanced diabetes) should also be taken into account. In addition, the hsCRP and PCT levels in patients with non-ulcer complaints increased and were greater than those in patients with ulcer-related complaints. In contrast, the median WBC count did not increase in either groups. On the one hand, this shows that different infection indicators may have different sensitivities to different infection parts; WBC might not be sensitive or accurate in evaluating the infection severity of DFU, as reported elsewhere.<sup>19,20</sup>

Before admission, a very low proportion of patients had been treated by a DF specialist or in a clinical setting with DF specialists. During this hospitalization, there were still some patients who did not receive a consultation of DF specialists. Patients with a newly developed DFU, worsening of the original ulcer or complicated with systemic diseases such as cardiac or renal disorders, need to be evaluated by DF specialists, and those (with either ulcer-related complaints or non-ulcer complaints) who are not treated by specialists in time (there is no uniform standard for the specific time) are



considered delayed in diagnosis and treatment.<sup>1,21,22</sup> The results of this study suggest that the primary reason for the diagnosis and treatment delay might be “patient delay”, and that “professional delay” caused by medical factors is the secondary reason. Unfortunately, even in a tertiary hospital with special multidisciplinary input for DF, up to one-fifteenth of inpatients still suffer from professional delay. There are many reasons for patient delay, which might be related not only to the ulcers’ hidden occurrence (lack of protective sensation) but also to the patients’ lack of medical knowledge and awareness of DF, not having confidence in treatment or not knowing where to visit.<sup>2,23</sup> In this study, the time interval from the discovery of ulcers to admission in patients with non-ulcer complaints was longer, and some were even unable to determine the exact period when their ulcers started. In addition, the high cost and uneven distribution of medical resources might be the reason.<sup>24</sup> In our study, more patients with non-ulcer complaints lacked basic medical insurance (Table 1). These data show the matters to some extent. The reasons for professional delay are more complicated, which may be related to the non-specialists’ lack of DFU care skills and insufficient attention. Furthermore, this might be attributed to a poorly structured DFU care network and an inefficient referral model between the non-specialists and specialists.<sup>2,24–26</sup> In this study, patients suffered from professional delay both before and after admission, which proves the universality of this phenomenon in clinical settings at various levels. In fact, diagnosis and treatment delay is common in China and even worldwide.<sup>1,2</sup> The implementation of the multidisciplinary team approach and the development of a system of tiered diagnosis and treatment have proven to be efficient.<sup>3,27–29</sup> However, it seems more difficult to improve the efficiency of the management of DFU patients with non-ulcer complaints. Whether more involved departments (such as non-endocrinology internal medicine departments) should be included in the multidisciplinary team for DF care or whether patients with the specific characteristics discussed above should be regarded as key targets need more exploration.

Approximately two-fifths of the DFU inpatients with non-ulcer complaints were Wagner grades 3–4 and IWGDF/IDSA grades 3 and above, but very few were referred for ulcer-related reasons during hospitalization. Why not referrals are related to the patient’s wishes and beliefs, such as disallowing amputation, and more importantly, the patient’s complex health condition. Which is more pressing, the management of local or systemic diseases? It is suggested that patients with DFU should be consulted or referred by DF specialists in time if the following conditions occur: sharp changes in skin color, local pain aggravated by inflammation, deterioration of original superficial ulcers involving soft tissue and/or bone tissue, signs of systemic infection, osteomyelitis, etc.<sup>1,20</sup> However, the absolute indications for emergency surgeries include only DFUs with serious or progressive infections (such as sepsis, infectious syndrome, necrotizing fasciitis and extensive wet gangrene), which are limb-threatening or even life-threatening.<sup>19,22,30</sup> In this study, patients with non-ulcer complaints had more coexisting diseases and worse organ function, as discussed above. Therefore, whether it is appropriate to implement aggressive surgical treatments for wounds or whether the benefits are greater than the risks remains to be discussed. In recent decades, the concept of palliative care has been introduced into the management of chronic wounds, including DFUs.<sup>31–34</sup> Symptom management is the core of palliative care and aims to alleviating patients’ suffering and improve their quality of life. The specific treatment objectives for DFU include reducing local exudation, eliminating odor, and relieving pain. However, at present, there are few discussions on the implementation indications and specific opportunities for palliative care. In the case of the following situations, palliative care might be considered:<sup>35–38</sup> (1) Coexisting diseases are serious (poor functional status, or very weak), and the treatment risk is high; terminal illness, and short life expectancy; the treatment benefit is small, and foot function could not be recovered. For example, severe heart failure, and RI of (eGFR) < 30 mL/(min·1.73m<sup>2</sup>), other critical diseases, advanced malignant tumors, long-term bedridden status, etc. (2) The chance of successful treatment is small: through full evaluation, it is determined that the current method can not heal the wound. In the whole management process of DF, palliative care and standard/usual care (suggested by guidelines) can be combined, and the two goals of “controlling symptoms” and “promoting healing” form a “dynamic balance” with the progress of the disease course.<sup>36</sup> This strategy is considered suitable for most chronic wounds. In other words, palliative care does not mean ‘no treatments’, and infection control, pressure off-loading, appropriate debridement and dressing changes, and glycemic control and treatment of comorbidities are still needed. In this study, a quarter of the patients with non-ulcer complaints did not receive local wound care after admission, and less than one-eighth of the patients received symptomatic analgesic treatment. This shows that many medical staff might have a biased understanding and not accept the concept of “wound

management in palliative care”, and still take “complete healing” as the only goal and ignore others, so they choose to give up when the purpose of complete healing seems impossible to achieve. The connotation of palliative care is very rich. DF specialists should still be responsible for grasping and communicating, and if necessary, palliative care specialists should be combined.<sup>36</sup> Palliative care pays more attention to the improvement in patients’ subjective feelings and quality of life, but this topic was not investigated in this study, which led to some important content being missing.

In this study, there was no significant difference in the short-term (in-hospital) outcomes between inpatients with ulcer-related and non-ulcer complaints. Patients with non-ulcer complaints have a milder severity of ulcers, but their prognosis is not better, at least significantly. The results suggest that treatments for these patients need to be improved substantially. However, there are limitations in the assessment of outcomes. First, we could not accurately judge the wound area according to the medical records, and the status of wound healing was only divided into three levels, which may have led to the underestimation of the difference in healing status between groups. Second, it is not comprehensive to use RWA% only to evaluate the healing status of wounds, especially those with deep tissue destruction, serious infection, and gangrene. In the follow-up, the long-term (out-of-hospital) survival rates of the two groups were not significantly different. The trends of the difference in mortality rates were more obvious early but gradually decreased approximately one year after discharge, while the opposite trend was observed for readmission rates. The long-term prognosis is influenced by more complex factors, especially the overall health status of patients. Among the patients with non-ulcer complaints, nearly a quarter of the readmitted patients were readmitted for DFU reasons at least once after the first discharge, and the total number of readmissions was greater. These findings suggest that their quality of life was obviously affected. However, the follow-up time of this study was relatively short. Prospective studies with larger sample sizes and longer follow-up times are needed to clarify more.

In this study, some DFU patients still did not effectively heal at discharge, and most of them were Wagner grades 3–4 at admission. Under what circumstances can the patients be discharged from the hospital? First, the stable local condition of DFU should be ensured (no signs of acute inflammation, no deep tissue destruction and no severe limb ischemia).<sup>4</sup> In clinical practice, for various reasons, it is difficult for inpatients with DFU Wagner grades 3–4, especially the latter two, to reach the above discharge indications. Whether adjusting the discharge indications for patients with poor basic functional status is more appropriate needs further exploration. Furthermore, a good discharge plan and post discharge management are needed.<sup>4,22</sup> Mastering this is particularly important for non-specialists.

Previously, there was limited evidence on DFU inpatients admitted with non-ulcer complaints, and the clinical characteristics of this population have not always been clearly known. This study fills the gap in the relevant information in this field. It describes and analyzes the clinical characteristics of previously widely neglected DFU patients with non-ulcer complaints and provides some reference for exploring solutions to problems in the DFU management process. In clinical practice, some measures might be considered to improve the situation, such as strengthening the guidance for focal populations, optimizing the structure of the multidisciplinary team and its operation process, and promoting the strategy of “wound management in palliative care”. However, notably, the subjects included in this study were DFU patients who were hospitalized after the outbreak of the COVID-19 epidemic (between August 2020 and January 31, 2023). The presentations and hospitalizations of DFUs clearly decreased early in the epidemic. Afterward, the hospitalizations recovered some ground, while the number of urgent admissions increased.<sup>39</sup> With respect to prognosis, the impact of the epidemic on amputation and mortality is complicated.<sup>40</sup> The limitation of this study is that we did not conduct a subgroup analysis by the date of admission and did not collect data before the COVID-19 epidemic for comparison. Therefore, we cannot clearly determine the specific impact of the epidemic on the results of this study. There are other limitations: (1) There may be cases of missed diagnosis or misdiagnosis of DF among patients admitted with non-ulcer complaints. Moreover, patients with non-ulcer complaints might have more missing information on wounds, such as the duration of ulcers. In fact, during the subject screening process, the majority (21 out of 23, un-presented) of the excluded patients missing important information came from patients with non-ulcer complaints. The exclusion of this population from the analyses may cause bias. (2) This is a single-center study conducted in a large district general hospital with a relatively high level of medical care. Things might be different or worse in areas with poor medical resources or hospitals with lower medical standards. (3) This study is retrospective, and the results should be interpreted with caution for potential confounding factors. Given all of the limitations above, the perspectives and conclusions drawn

from this study are preliminary. Further multi-center prospective studies with larger sample sizes and longer follow-up times are needed to verify these findings.

## Conclusion

Approximately one-third of inpatients with DFU are admitted with non-ulcer complaints, and most of them are admitted to departments without DF specialists. Inpatients with non-ulcer complaints have milder wounds but more severe and greater comorbidities and worse organ function. These patients do not receive standardized management for DFU either before or after admission. Targeted measures are needed to improve this situation.

## Abbreviations

ABI, ankle-brachial index; ALB, albumin; Crea, creatinine; ALT, alanine aminotransferase; AKI, acute kidney injury; AST, aspartate aminotransferase; BP, blood pressure; CAD, coronary artery disease; DKA, diabetic ketoacidosis; CKD, chronic kidney disease; DF, diabetic foot; DFU, diabetic foot ulcer; DP, diastolic pressure; DPN, diabetic peripheral neuropathy; FBG, fasting blood glucose; Hb, hemoglobin; HbA1c, glycosylated hemoglobin A1c; HDL-C, high density lipoprotein-cholesterol; HHS, hyperosmolar hyperglycemia syndrome; hsCRP, hypersensitive C reactive protein; ICD, International Classification of Disease; IDSA, Infectious Diseases Society of America; IQR, interquartile range; IWGDF, International Working Group on Diabetic Foot; KDIGO, Kidney Disease Improving Global Outcomes; LDL-C, low density lipoprotein-cholesterol; PAD, peripheral arterial disease; PCT, procalcitonin; PRD, progressive renal disease; RI, renal insufficiency; RWA, reduction in wound area; SP, systolic pressure; TC, total cholesterol; TG, triglyceride; WBC, white blood cell.

## Data Sharing Statement

The datasets generated during this study are available from the correspondences on reasonable request. This paper has been uploaded to ResearchSquare as a preprint: <https://www.researchsquare.com/article/rs-3746261/v1>.

## Ethics Approval

The Medical Ethical Review Board of the Second People's Hospital of Chengdu approved this study (Approval No. 2023385). All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

## Informed Consent

The need for written informed consent was waived by the Medical Ethical Review Board of the Second People's Hospital of Chengdu due to retrospective nature of the study. Throughout the research process, we have adhered strictly to medical ethical guidelines, ensuring compliance and respecting patients' privacy rights. Patient data is exclusively used for the purposes outlined in this study and will not be utilized for any commercial activities, advertising, or purposes unrelated to the research objectives without explicit consent from the patient or their legal representative. The data used in this study was anonymized.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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# Disclosure

The authors report no conflicts of interest in this work.

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