ISSN 1948-9358 (online)

World Journal of *Diabetes*

World J Diabetes 2024 October 15; 15(10): 2002-2156

Published by Baishideng Publishing Group Inc

World Journal of Diabetes

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ABOUT COVER

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RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Diabetes

ISSN
ISSN 1948-9358 (online)

LAUNCH DATE
June 15, 2010

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Lu Cai, Md. Shahidul Islam, Michael Horowitz

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-9358/editorialboard.htm

PUBLICATION DATE
October 15, 2024

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World Journal of Diabetes

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World J Diabetes 2024 October 15; 15(10): 2070-2080

DOI: 10.4239/wjd.v15.i10.2070

ISSN 1948-9358 (online)

ORIGINAL ARTICLE

Retrospective Study

Delayed treatment of diabetic foot ulcer in patients with type 2 diabetes and its prediction model

Hui Chen, Ying Xi

Specialty type: Endocrinology and metabolism

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade C, Grade C

Novelty: Grade B, Grade B

Creativity or Innovation: Grade B, Grade C

Scientific Significance: Grade B, Grade C

P-Reviewer: Dabla PK; Lorusso F; Rapone B

Received: July 23, 2024

Revised: August 19, 2024

Accepted: September 2, 2024

Published online: October 15, 2024

Processing time: 64 Days and 18.8 Hours

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Abstract

BACKGROUND

Diabetic foot (DF) is a serious complication of type 2 diabetes. This study aimed to investigate the factors associated with DF occurrence and the role of delayed medical care in a cohort of patients with type 2 diabetes.

AIM

To reveal the impact of delayed medical treatment on the development of DF in patients with type 2 diabetes and to establish a predictive model for DF.

METHODS

In this retrospective cohort study, 292 patients with type 2 diabetes who underwent examination at our hospital from January 2023 to December 2023 were selected and divided into the DF group (n = 82, DF) and nondiabetic foot group (n = 210, NDF). Differential and correlation analyses of demographic indicators, laboratory parameters, and delayed medical treatment were conducted for the two groups. Logistic regression was applied to determine influencing factors. Receiver operating characteristic (ROC) analysis was performed, and indicators with good predictive value were selected to establish a combined predictive model.

RESULTS

The DF group had significantly higher body mass index (BMI) ($P < 0.001$), disease duration ($P = 0.012$), plasma glucose levels ($P < 0.001$), and HbA1c ($P < 0.001$) than the NDF group. The NDF group had significantly higher Acute Thrombosis and Myocardial Infarction Health Service System (ATMHSS) scores ($P < 0.001$) and a significantly lower delayed medical treatment rate (72.38% *vs* 13.41%, $P < 0.001$). BMI, duration of diabetes, plasma glucose levels, HbA1c, diabetic peripheral neuropathy, and nephropathy were all positively correlated with DF occurrence. ATMHSS scores were negatively correlated with delayed time to seek medical treatment. The logistic regression model revealed that BMI, duration of diabetes, plasma glucose levels, HbA1c, presence of diabetic peripheral neuropathy and

nephropathy, ATMHSS scores, and delayed time to seek medical treatment were influencing factors for DF. ROC analysis indicated that plasma glucose levels, HbA1c, and delayed medical treatment had good predictive value with an area under the curve of 0.933 for the combined predictive model.

CONCLUSION

Delayed medical treatment significantly affects the probability of DF occurrence in patients with diabetes. Plasma glucose levels, HbA1c levels, and the combined predictive model of delayed medical treatment demonstrate good predictive value.

Key Words: Delayed treatment; Medical attention; Diabetic foot ulcer; Type 2 diabetes; Prediction model

Core Tip: This retrospective cohort study investigates factors influencing diabetic foot (DF) in type 2 diabetes patients. Key findings highlight that increased body mass index, longer diabetes duration, elevated plasma glucose and HbA1c levels, as well as complications like diabetic neuropathy, are positively associated with DF occurrence. Additionally, a low Attitudes Toward Medical Help Seeking Scale score and delayed medical care over 3 months correlate with DF. These insights underscore the importance of proactive diabetes management and timely medical intervention to prevent DF, with the study's predictive model demonstrating strong diagnostic potential (area under the curve = 0.933).

Citation: Chen H, Xi Y. Delayed treatment of diabetic foot ulcer in patients with type 2 diabetes and its prediction model. *World J Diabetes* 2024; 15(10): 2070-2080
URL: https://www.wjgnet.com/1948-9358/full/v15/i10/2070.htm
DOI: https://dx.doi.org/10.4239/wjd.v15.i10.2070

INTRODUCTION

Type 2 diabetes is a long-term condition marked by the body's inability to properly use insulin or a reduced efficiency in insulin function, leading to persistently elevated blood sugar levels. Its epidemiological characteristics vary by region and population and are associated with genetic, lifestyle, and environmental factors[1,2]. Its typical manifestations include polyuria, polydipsia, polyphagia, and weight loss. Prolonged hyperglycemia can cause the occurrence and development of various complications[3,4].

Diabetic foot (DF) is a serious diabetes-related complication involving nerve damage in the lower extremities and various levels of vascular disease. This condition can cause infections, ulcers, and serious damage to deep tissues in patients. Severe symptoms can result in difficulty walking and even amputation, significantly influencing the quality of life of patients with diabetes[5,6]. At present, the cure rate for DF is improving and the amputation rate is gradually decreasing; however, its incidence is increasing year by year[7,8].

Delay in seeking medical care is defined as the behavior of individuals who do not seek timely medical care after discovering abnormal bodily symptoms due to objective or subjective reasons. This behavior occurs because the early symptoms of DF are not evident, and patients with diabetes do not actively seek foot examinations at hospitals to assess their risk of developing DF[9,10]. As a consequence, delayed medical care often leads to DF.

Although previous studies have analyzed the risk factors for DF[11-13], no research has focused on the impact of delayed medical care on the probability of DF occurrence in patients with diabetes. Therefore, investigating the impact of delayed medical care on DF occurrence in patients with diabetes is of utmost importance.

MATERIALS AND METHODS

Study design

This retrospective cohort study included 292 individuals diagnosed with type 2 diabetes who received examinations at our hospital over the period from January 2023 to December 2023. They were divided into the DF group (n = 82) and nondiabetic foot group (n = 210, NDF group). This study was approved by the institutional review board and ethics committee of Shaanxi Provincial People's Hospital. Given its retrospective design, this study only used data from unidentified patients and informed consent was waived.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Diagnosis of type 2 diabetes as per World Health Organization guidelines[14]; (2) Aged between 18 and 80 years; and (3) Ineligibility for surgical revascularization.

The exclusion criteria were as follows: (1) Prior occurrence of acute coronary syndrome, myocardial infarction, or transient ischemic stroke within the last 6 months; (2) Presence of uncontrolled immune disorders or active severe systemic infections; (3) Severe hematologic disorders or coagulation abnormalities; (4) History of malignant tumors; (5) Participation in other clinical trials within the preceding 3 months; or (6) Other concerns identified by the investigators that may impede compliance or safety.

The patients were grouped based on the presence or absence of DF: DF group (n = 82) and NDF group (n = 210). The diagnostic criteria were based on the 2012 Infectious Diseases Society of America clinical practice guidelines for DF infections[14].

Data collection

Patient demographic data were acquired from the medical records system. Upon admission, 5 mL of fasting blood sample was obtained from the antecubital vein in the morning for blood testing. Hematological parameters such as hemoglobin (g/dL), hematocrit (%), white blood cell count (× 10^9/L), and platelet count (× 10^9/L) were measured using a fully automated coagulation analyzer (HC00608166, STA Compact, China).

Biochemical parameters and genomic and proteomic data were analyzed using venous blood samples of 5-7 mL (including whole blood, plasma, and serum). The measured biochemical markers included HbA1c, plasma glucose, total cholesterol (measured by the CHOD-PAP method), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, urea, and creatinine. All quantitative measurements were performed using a BS 400 auto-analyzer in accordance with the procedures provided by Dia Sys Diagnostic Systems GmbH, Germany. The glomerular filtration rate (GFR) was computed from serum creatinine levels using the formula: GFR (mL/minute/1.73 m^2) = (140 - age) × weight (kg)/72 × serum creatinine (mg/dL).

Delay in seeking medical care

Delay in seeking medical care (patient delay) refers to the behavior of individuals who fail to seek timely medical attention after noticing abnormal symptoms due to objective or subjective reasons. The time of medical delay is defined as the interval between the time the patient first noticed the symptoms and their first visit to a healthcare facility, with a duration of over 3 months considered as medical delay.

Attitudes Toward Medical Help Seeking Scale (ATMHSS): The ATMHSS is a self-assessment scale consisting of 35 items divided into four dimensions: Behavioral intention (12 items), nonfatalism (11 items), medical trust (7 items), and nonavoidant attitudes (5 items). Each item is rated on a Likert 4-point scale, with “disagree” to “agree” corresponding to scores of 0-3. The total score ranges from 0 to 105, where a high score indicates a positive attitude toward seeking medical care. The scale has a Cronbach's α coefficient of 0.82.

Sample size and statistical power

The sample size was mainly depended on the number of patients included in the inclusion time frame complied with the events per variable > 10 principle. Using G*Power 3.1.9.7, we conducted a *post hoc* analysis based on the "Means: Difference between two independent means (two groups)" option for t-tests. We configured the analysis with a two-tailed mode, an effect size of d = 0.6, and a significance level (α err prob) of 0.05. After inputting the sample sizes for the two groups, we calculated the power (1 - β err prob), which yielded a result of 0.969.

Statistical analysis

Patient characteristics were compared between the two groups using independent t-tests for continuous variables and χ^2 tests for categorical variables. The normality of continuous variables was checked using the Shapiro-Wilk test. Normally distributed data were expressed as mean ± SD, and categorical variables were reported as counts and percentages. A P value of less than 0.05 was deemed statistically significant. All analyses were conducted with SPSS software, version 29.0 (SPSS Inc., Chicago, IL, United States).

Spearman correlation analysis was conducted. Indicators showing significant differences in the differential and correlation analyses were included as covariates in logistic regression analysis. The diagnostic efficiency of delayed medical care for DF was assessed using the area under the receiver operating characteristic (ROC) curve, and a combined predictive model was established by incorporating blood glucose levels, glycated protein levels, and delayed medical care.

RESULTS

Demographic characteristics

Between-group comparison showed no statistically significant differences in general demographic data such as age and gender in the presence of DF (P > 0.05; Table 1). However, the body mass index (BMI) of the DF group was significantly higher than that of the NDF group (23.51 ± 3.57 *vs* 25.17 ± 3.57, P < 0.001). This finding suggests that an increase in BMI may elevate the incidence of DF.

Table 1 Comparison of general demographic data, *n* (%)

Characteristic	NDF group (*n* = 210)	DF group (*n* = 82)	t/χ^2	*P* value
Age (years)	51.15 ± 9.32	52.69 ± 9.15	1.283	0.201
BMI (kg/m^2)	23.51 ± 3.57	25.17 ± 3.57	3.588	< 0.001
Sex	107 (50.95)	47 (57.32)	0.720	0.396
Smoking history	51 (24.29)	19 (23.17)	0.295	0.587
Alcohol history	65 (30.95)	24 (29.27)	0.060	0.807
Family history of diabetes	44 (20.95)	21 (25.61)	0.150	0.699
Hypertension	39 (18.57)	18 (21.95))	1.229	0.268
Hyperlipidemia	37 (17.62)	16 (19.51)		

BMI: Body mass index; DF: Diabetic foot; NDF: Nondiabetic foot group.

Diabetes-related indicators and complications

Differential analysis was conducted on the occurrence probabilities of diabetes duration, classification, staging, and complications between the two groups (Table 2). No significant differences were observed in classification, staging, diabetic retinopathy, and diabetic vascular disease ($P > 0.05$). The duration of diabetes in the DF group was significantly longer than that in the NDF group (10.12 ± 4.95 *vs* 11.74 ± 4.84, $P = 0.012$). In addition, the occurrence rates of diabetic neuropathy (22.86% *vs* 40.2%, $P = 0.005$) and diabetic nephropathy (0.48% *vs* 4.88%, $P = 0.035$) were markedly lower in the NDF group compared with those in the DF group. These findings suggest that an increase in diabetes duration and the occurrence of some complications may contribute to the increased incidence of DF.

Routine blood examination

Routine blood examination indicated no statistical differences in hemoglobin concentration, white blood cell count, red blood cell count, neutrophil count, and platelet count between the two groups ($P > 0.05$; Figure 1). This finding suggests that preoperative blood routine indicators have no impact on the research results.

Blood glucose and lipid levels

Examination of the patients' blood glucose and lipid levels indicated no statistical differences in total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol between the two groups ($P > 0.05$; Figure 2). This finding suggests that preoperative blood routine indicators have no impact on the research results. However, the DF group exhibited significantly higher levels of plasma glucose (5.71 ± 0.61 *vs* 10.24 ± 4.72, $P < 0.001$) and HbA1c (7.41 ± 1.87 *vs* 9.12 ± 1.65, $P < 0.001$) than the NDF group. This result indicates that elevated blood glucose levels have a negative impact on DF occurrence.

Renal function levels

Differential analysis was conducted on the renal function indicators of the two groups, including plasma creatinine, plasma urea, and estimated GFR (Table 3). No significant differences in renal function indicators were found between the two groups ($P > 0.05$). This finding suggests that intraoperative indicators have no impact on the research results.

Delayed medical care

The patients' delayed medical care of more than 3 months was recorded, and their willingness to seek medical care was assessed using the ATMHSS (Table 4). The NDF group had significantly higher ATMHSS scores (68.71 ± 10.41 *vs* 59.84 ± 9.78, $P < 0.001$) and lower rate of delayed medical care (13.41% *vs* 72.38%) compared with the DF group. This finding indicates that low willingness to seek medical care and delayed medical care may lead to DF.

Correlation analysis

A significant correlation was observed between various indicators and DF occurrence (Table 5). On the one hand, BMI, duration of diabetes, plasma glucose, HbA1c, and presence of diabetic peripheral neuropathy and diabetic nephropathy were positively correlated with DF occurrence. On the other hand, the ATMHSS score and duration of medical delay were negatively correlated with DF occurrence. These results underscore the predictive potential of these indicators for DF occurrence.

Logistic regression analysis

Logistic regression analysis revealed a significant finding (Table 6). The multivariate regression model demonstrated that BMI, duration of diabetes, plasma glucose, HbA1c, presence of diabetic peripheral neuropathy and diabetic nephropathy, ATMHSS score, and medical delay time all had a strong diagnostic value for DF.

Table 2 Diabetes-related indicators and complications, *n* (%)

Characteristic		NDF group (*n* = 210)	DF group (*n* = 82)	t/χ^2	*P* value
Duration of diabetes (years)		10.12 ± 4.95	11.74 ± 4.84	2.554	0.012
Types	Insulin resistance	179 (85.24)	70 (85.37)	0.000	1.000
	Insufficient insulin secretion	31 (14.76)	12 (14.63)		
Stages	Impaired glucose tolerance	29 (13.81)	11 (13.41)	0.008	0.996
	Type 2 diabetes stage	120 (57.14)	47 (57.32)		
	Late stage of type 2 diabetes	61 (29.05)	24 (29.27)		
Diabetic retinopathy		43 (20.48)	24 (29.27)	2.105	0.147
Diabetic vascular disease		69 (32.86)	30 (36.59)	0.218	0.640
Diabetic peripheral neuropathy		48 (22.86)	33 (40.24)	8.048	0.005
Diabetic nephropathy		1 (0.48)	4 (4.88)	4.426	0.035

DF: Diabetic foot; NDF: Nondiabetic foot group.

Table 3 Renal function levels, *n* (%)

Characteristic	NDF group (*n* = 210)	DF group (*n* = 82)	t/χ^2	*P* value
Plasma creatinine (μmol/L)	49.7 ± 4.12	50.27 ± 4.34	1.024	0.307
Plasma urea (mmol/L)	1.35 ± 0.59	1.41 ± 0.67	0.687	0.493
eGFR, mL/min/1.73 m^2			0.048	0.827
≥ 60	153 (72.86)	58 (70.73)		
< 60	57 (27.14)	24 (29.27)		

DF: Diabetic foot; NDF: Nondiabetic foot group; eGFR: Estimated glomerular filtration rate.

Table 4 Delayed medical care, *n* (%)

Characteristic		NDF group (*n* = 210)	DF group (*n* = 82)	t/χ^2	*P* value
ATMHSS score		68.71 ± 10.41	59.84 ± 9.78	6.84	< 0.001
Medical delay time	Less than 3 months	152 (72.38)	11 (13.41)	80.773	< 0.001
	More than 3 months	58 (27.62)	71 (86.59)		

DF: Diabetic foot; NDF: Nondiabetic foot group; ATMHSS: Acute thrombosis and myocardial infarction health service system.

ROC analysis

A validation cohort of patients was used to establish a predictive model for DF occurrence based on factors such as BMI, duration of diabetes, blood glucose levels, complications, and medical delay (Table 7). The results demonstrated that plasma glucose [area under the curve (AUC) = 0.819], HbA1c (AUC = 0.804), and medical delay (AUC = 0.795) exhibited good predictive value. The combined predictive model yielded an AUC of 0.933 (Figure 3).

DISCUSSION

Diabetes represents an increasingly growing public health concern, with its associated complications drawing increasing attention[15,16]. Owing to the global prevalence of diabetes and the increased life expectancy of patients with diabetes, the incidence of DF has risen. Diabetes-related foot complications are one of the most common complications among patients with diabetes, constituting a significant healthcare burden[17-19].

Table 5 Correlation analysis

Characteristic	Rho	*P* value
BMI (kg/m^2)	0.206	< 0.001
Duration of diabetes (years)	0.147	0.012
Plasma glucose	0.626	< 0.001
HbA1c (%)	0.498	< 0.001
ATMHSS score	-0.364	< 0.001
Diabetic peripheral neuropathy	0.175	0.003
Diabetic nephropathy	0.152	0.009
Medical delay time	-0.534	< 0.001

BMI: Body mass index; ATMHSS: Acute thrombosis and myocardial infarction health service system.

Table 6 Logistic regression analysis

	Coef	Odds ratio	B	Beta	*P* value
BMI (kg/m^2)	0.130	1.139	3.440	0.130	< 0.001
Duration of diabetes (years)	0.067	1.069	2.481	0.067	0.013
Plasma glucose	0.775	2.171	6.459	0.775	< 0.001
HbA1c (%)	0.902	2.463	7.363	0.902	< 0.001
ATMHSS score	0.083	0.921	5.770	-0.083	< 0.001
Diabetic peripheral neuropathy	0.821	2.273	2.945	0.821	0.003
Diabetic nephropathy	2.372	10.718	2.107	2.372	0.035
Medical delay time	2.828	0.059	7.88	-2.828	< 0.001

BMI: Body mass index; ATMHSS: Acute thrombosis and myocardial infarction health service system.

Table 7 Receiver operating characteristic analysis

	Sensitivities	Specificities	AUC	Youden index
BMI (kg/m^2)	0.573	0.633	0.631	0.206
Duration of diabetes (years)	0.463	0.714	0.597	0.177
Plasma glucose	0.720	1.000	0.819	0.720
HbA1c (%)	0.646	0.867	0.804	0.513
ATMHSS score	0.646	0.700	0.731	0.346
Diabetic peripheral neuropathy	0.402	0.771	0.587	0.173
Diabetic nephropathy	0.049	0.995	0.522	0.044
Medical delay time	0.866	0.724	0.795	0.590

BMI: Body mass index; ATMHSS: Acute thrombosis and myocardial infarction health service system; AUC: Area under the curve.

Patient delay in seeking medical attention may result in the disease being in an advanced stage at the time of diagnosis. Medical delay can significantly reduce the clinical effectiveness of treatment, increase the treatment burden on patients, and even impact their short- and long-term prognoses.

The primary finding of this study is the impact of medical delay on the incidence of DF. Between-group comparison of the probability of medical delay and patients' willingness to seek medical care revealed that patients with medical delay and low willingness to seek medical care may have an increased likelihood of developing DF. The possible underlying mechanism is that patient delay in seeking medical attention may lead to the disease being in an advanced stage at the

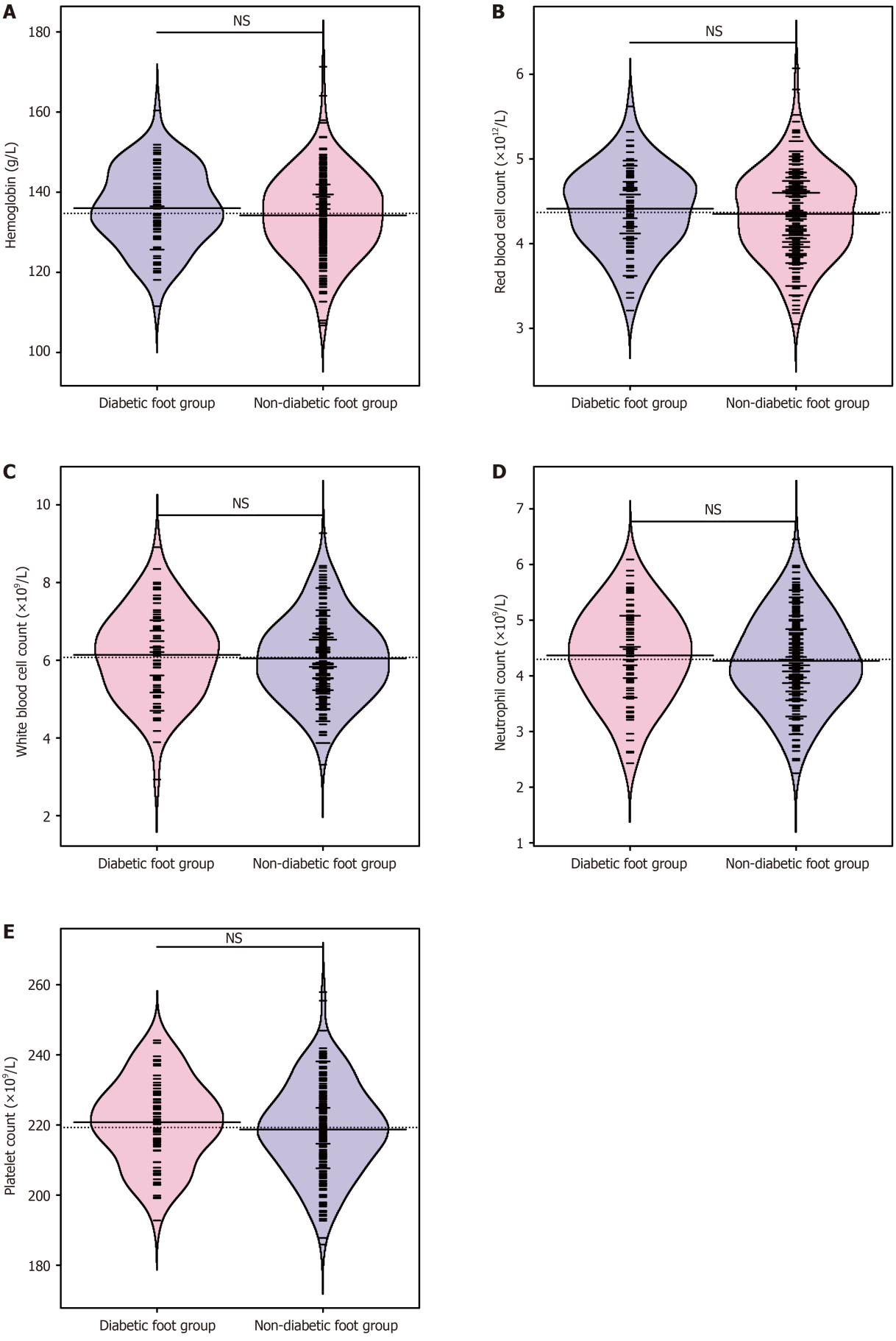

Figure 1 Blood Routine Examination. A: Hemoglobin concentration; B: Red blood cell count; C: White blood cell count; D: Neutrophil count; E: Platelet. NS: No significant difference.

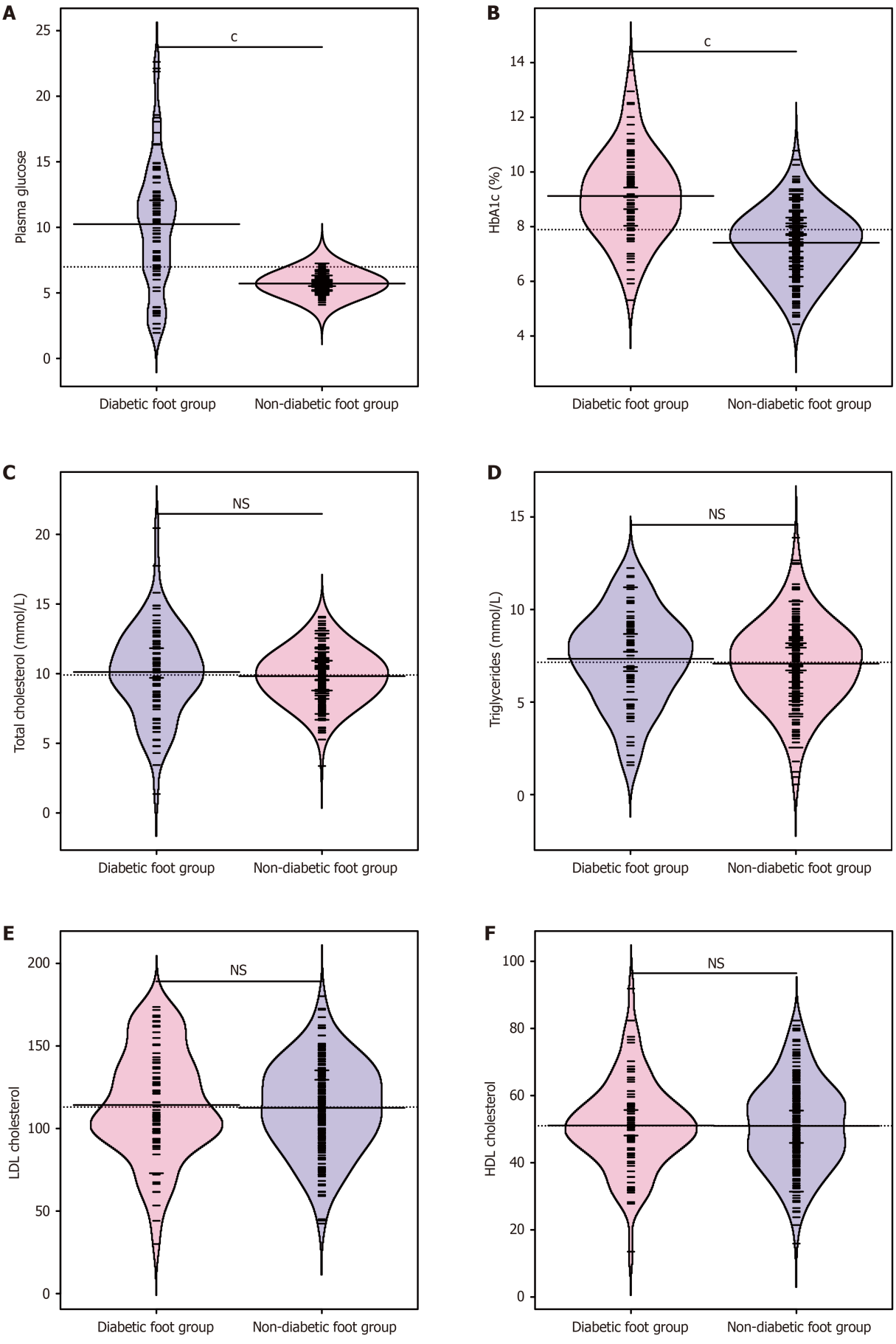

Figure 2 Blood glucose and lipid levels. A: Plasma glucose; B: HbA1c; C: Total cholesterol; D: Triglycerides; E: Low-density lipoprotein cholesterol; F: High-density lipoprotein cholesterol. $^{c}P < 0.001$; NS: No significant difference.

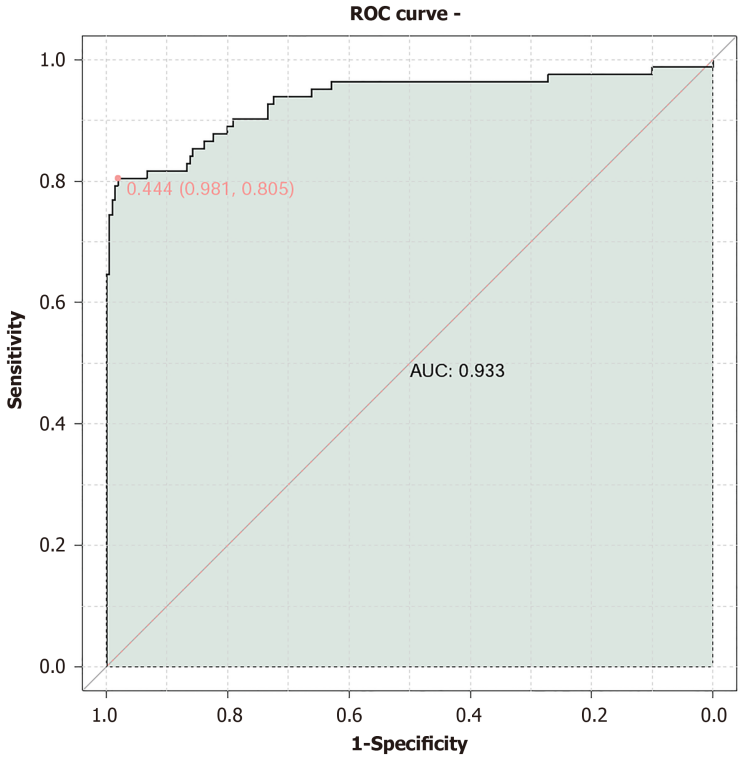

Figure 3 Analysis of the combined predictive model for plasma glucose, HbA1c, and medical delay. ROC: Receiver operating characteristic; AUC: Area under the curve.

time of diagnosis, significantly reducing the clinical effectiveness of treatment, increasing the treatment burden on patients, and possibly affecting their short- and long-term prognoses. The low willingness of patients to seek medical care may be due to inadequate education, insufficient awareness of DF prevention, and lack of habit of timely check-ups and medical care[20,21]. In addition, the early symptoms of DF, such as coolness in the soles of the feet and delayed sensation, are often subtle and easily overlooked by patients, leading to medical delay.

Furthermore, the results of this study indicate that BMI, plasma glucose, and HbA1c levels are associated with DF. This relationship may be related to poor control of blood glucose levels in patients, leading to vascular changes in the lower extremities, insufficient blood supply to the lower limbs, and ultimately the occurrence of DF[22-24]. Chen *et al*[25] also illustrated that uncontrolled blood glucose levels in patients with diabetes can lead to diabetic complications. Consistent with the present findings, high blood glucose levels are associated with severe DF ulcers[25].

Diabetic neuropathy can affect the central and peripheral nervous systems, with the latter being particularly common. In particular, distal sensory neuropathy is the most prevalent and accounts for over 50% of all diabetic neuropathies[26,27]. Diabetic nephropathy is one of the most significant complications in patients with diabetes and often concurrently involves microvascular disease in other organs or systems[28,29]. Although the correlation of certain complications such as diabetic retinopathy and DF with diabetes is relatively low, the occurrence of diabetic neuropathy and diabetic nephropathy is significantly associated with DF. As the duration of diabetes progresses, the incidence of DF also increases.

BMI, duration of diabetes, plasma glucose, HbA1c, and presence of diabetic peripheral neuropathy and diabetic nephropathy are all positively correlated with DF occurrence. Meanwhile, the ATMHSS score and delayed medical care are negatively correlated with DF occurrence. Logistic regression analysis indicates that these factors are risk factors for DF. ROC analysis demonstrates that the combined predictive model of blood glucose levels and delayed medical care has good predictive value.

This study investigates the predictive role of delayed medical care and other factors in patients with DF. However, it has certain limitations. First, the retrospective design imposes inherent constraints on causal inferences, as the observed correlation between personalized care interventions and postoperative outcomes does not establish a clear causal relationship. The reliance on retrospective data collection also introduces the possibility of information bias and confounding variables that may impact the observed results. In addition, the limited sample size may restrict the applicability of the results to a broad patient population. For future research endeavors, we aim to carry out multicenter prospective studies to comprehensively investigate the influence of delayed medical care on the incidence of DF.

CONCLUSION

Delayed medical care significantly influences the likelihood of DF occurrence in patients with diabetes. The combined predictive model of plasma glucose, HbA1c levels, and delayed medical care demonstrates good predictive value.

FOOTNOTES

Author contributions: Chen H designed the experiments and conducted clinical data collection; Xi Y performed postoperative follow-up and recorded the data; Chen H and Xi Y conducted the collation and statistical analysis, wrote the original manuscript and revised the paper; Both authors read and approved the final manuscript.

Institutional review board statement: This study was approved by the institutional Review Board and Ethics Committee of Shaanxi Provincial People's Hospital.

Informed consent statement: The ethics committee agrees to waive informed consent.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: All data generated or analyzed during this study are included in this published article.

Country of origin: China

ORCID number: Ying Xi 0009-0003-5447-2847.

S-Editor: Li L
L-Editor: A
P-Editor: Zhao YQ

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