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*Original Article*

# Design and clinical application of a risk prediction model for diabetic foot

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**Abstract:** Objective: To construct and evaluate a nomogram prediction model for the risk of diabetic foot in patients with type 2 diabetes based on their clinical data, and to assist clinical healthcare professionals in identifying high-risk factors and developing targeted intervention measures. Methods: We retrospectively collected clinical data from 478 hospitalized patients with type 2 diabetes at the First Affiliated Hospital of Shantou University Medical College from January 2019 to December 2021. The patients were divided into a diabetic foot group (n=312) and a non-diabetic foot group (n=166) based on whether they had diabetic foot. The baseline data of both groups were collected. Univariate and multivariate analyses as well as logistic regression analysis were conducted to explore the risk factors for diabetic foot. A nomogram prediction model was established using the package "rms" version 4.3. The model was internally validated using the area under the receiver operating characteristic curve (AUC). Additionally, the decision curve analysis (DCA) was performed to evaluate the performance of the nomogram model. Results: The results from the logistic regression analysis revealed that being male, smoking, duration of diabetes, glycated hemoglobin, hyperlipidemia, and atherosclerosis were influencing factors for diabetic foot (all $P<0.05$). The AUC of the model in predicting diabetic foot was 0.804, with a sensitivity of 75.3% and specificity of 74.4%. Harrell's C-index of the nomogram prediction model for diabetic foot was 0.804 (95% CI: 0.762-0.844), with a threshold value of >0.675. The DCA findings demonstrated that the nomogram model provided a net clinical benefit. Conclusion: The nomogram prediction model constructed in this study showed good predictive performance and can provide a basis for clinical workers to prevent and intervene in diabetic foot, thereby improving the overall diagnosis and treatment.

**Keywords:** Diabetes, diabetic foot, nomogram prediction model, clinical application

## Introduction

Diabetes is a common chronic disease worldwide, characterized by insulin deficiency in the blood due to dysfunction of pancreatic islet cells, which in turn affects the body's ability to utilize glucose and ultimately results in clinical symptoms such as emaciation, polydipsia, polyuria, and polyphagia, severely impacting the patients' quality of life [1-3]. In addition, as the disease progresses, patients may develop vascular complications, including coronary heart disease, ocular blood flow abnormalities, and lower extremity vascular disease. Among them, distal lower extremity vascular lesions can cause foot ulcers or deep tissue damage, with or without infection [4]. Research has shown that diabetic necrosis is a serious public health problem worldwide [5]. Diabetic foot refers to infections, ulcers, or tissue damage in the feet of diabetic patients, often accompanied by peripheral neuropathy and/or peripheral arterial disease [6]. Severe cases can be challenging to treat, with a high risk of recurrence and potential for limb amputation. Therefore, predicting the risk factors for diabetic foot is of great clinical significance in reducing the incidence of necrosis.

The nomogram prediction model is a type of clinical prognostic prediction model and scoring system. It calculates a total score based on the numerical values of individual predictive variables, which is then used to estimate the risk or probability of a specific clinical event outcome. It has been proven to be effective in predicting the risk of various diseases. Although research on diabetic foot has made progress, consider-

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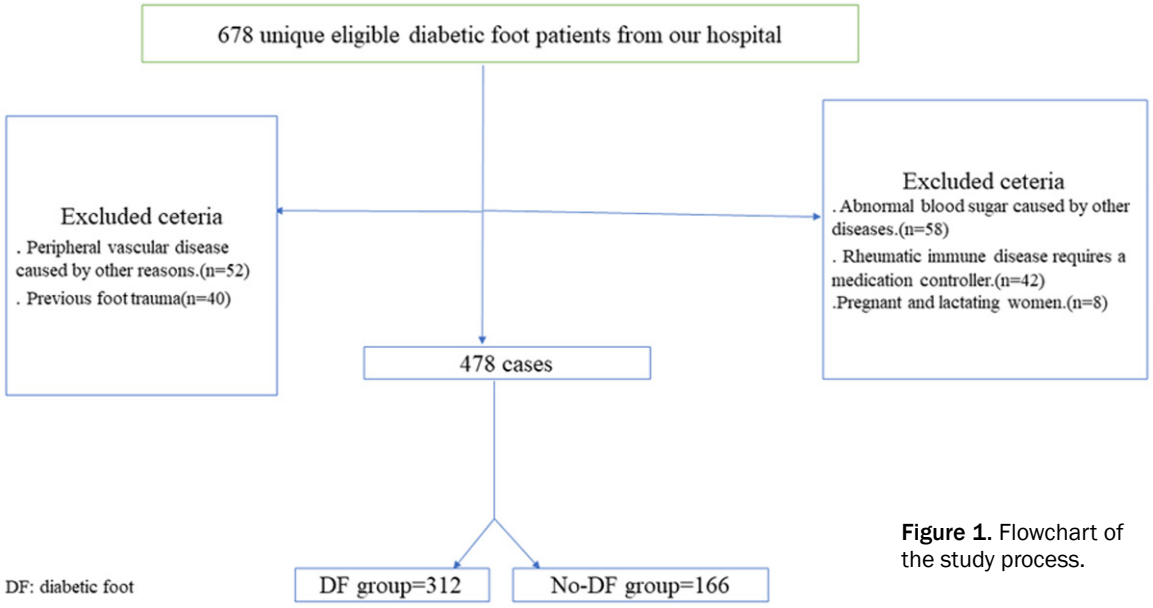


**Figure 1.** Flowchart of the study process.

ing the regional variations in the prevalence of diabetes and diverse lifestyle habits across different regions, developing specific prediction models for each locality is crucial for improving disease prevention [7, 8]. Based on the above theory, this study aims to identify the independent influencing factors associated with diabetic foot and construct a nomogram prediction model, providing more research targets for clinical intervention in diabetic necrosis.

## Materials and methods

### *General data*

The clinical data of 478 hospitalized patients with type 2 diabetes at the First Affiliated Hospital of Shantou University School of Medicine from January 2019 to December 2021 were retrospectively collected. The patients were divided into a diabetic foot group (n=312) and a non-diabetic foot group (n=166) based on whether they had diabetic foot (**Figure 1**).

Inclusion criteria: 1. Patients who met the diagnostic criteria for diabetic foot according to relevant guidelines, including abnormal foot sensation, foot deformities, ischemic pain, difficulty walking, with or without infection, ulcers, and gangrene, and early signs such as decreased skin temperature and pain [9]; 2. Patients with complete clinical data; 3. Patients who were treated for diabetic foot at The First Affiliated Hospital of Shantou University Medical College.

Exclusion criteria: 1. Patients with peripheral vascular diseases caused by other reasons; 2. Patients with previous foot trauma; 3. Patients with abnormal blood glucose levels caused by other diseases; 4. Patients with rheumatic immune diseases requiring medication; 5. Pregnant and lactating women.

The study was approved by the Ethics Committee of the First Affiliated Hospital of Shantou University Medical College.

### *Data collection*

General information of all patients, including gender, age, duration of diabetes, smoking history (≥1 cigarette per day for at least 6 months), alcohol consumption (≥50 mL per day), comorbidities, and body mass index (BMI), were collected through the electronic medical record system.

### *Hematologic values*

Serum indicators were traced back to the first hospitalization of all patients, including glycated hemoglobin, fasting blood glucose, lipid profile (cholesterol, triglycerides, high-density lipoprotein), pancreatic function indicator (C-peptide), liver function indicators (alanine aminotransferase, aspartate aminotransferase), renal function indicators (creatinine, blood urea nitrogen), routine blood indexes, coagulation function indicators, and nutritional indica-

**Table 1.** Comparison of baseline characteristics between the two groups

| Item | Diabetic foot group (n=322) | Non-diabetic foot group (n=166) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Gender | | | 5.634 | 0.018 |
| Male | 199 | 84 | | |
| Female | 123 | 82 | | |
| Age (years) | 65.5±8.4 | 64.9±8.3 | 0.751 | 0.453 |
| Body mass index (kg/m$^2$) | 22.7±1.6 | 23.1±1.5 | 2.672 | 0.080 |
| Alcohol history | 98 | 36 | 3.451 | 0.063 |
| Volume (mL/d) | 125.6±1.8 | 124.8±1.7 | 3.089 | 0.053 |
| Time of duration (years) | 13.4±4.9 | 13.8±5.2 | 0.664 | 0.077 |
| Smoking history | 100 | 27 | 12.447 | 0.000 |
| Volume (pcs/d) | 11.6±3.4 | 12.0±4.1 | 0.572 | 0.091 |
| Time of duration (years) | 25.4±4.3 | 26.2±3.9 | 1.889 | 0.641 |
| Hyperlipidemia | 87 | 14 | 23.050 | 0.000 |
| Coronary heart disease | 17 | 5 | 1.308 | 0.253 |
| Chronic obstructive pulmonary disease | 13 | 6 | 0.052 | 0.820 |
| Duration (year) | 3.23±1.4 | 3.42±1.3 | 1.419 | 0.364 |
| Duration of diabetes (year) | 15.8±2.2 | 13.8±2.4 | 9.221 | 0.000 |
| Hypertension | 45 | 23 | 6.830 | 0.671 |
| Duration (year) | 6.77±1.91 | 6.82±1.87 | 3.556 | 0.440 |
| Atherosclerosis | 71 | 19 | 8.188 | 0.004 |

Note: t: data from t-test; $\chi^2$: data from chi-square test.

tors (total bile acid, prealbumin, total serum protein).

Before blood collection, patients were instructed to fast and abstain from food, drink, and medication for at least 10 hours. The next morning, 5 ml of fasting blood was collected from each patient. After centrifugation at 3000 rpm for 10 minutes using a TD3WS centrifuge (Xiangmaida, instrument number 20160115), the serum was obtained and analyzed using a fully automated biochemical analyzer, employing oxidase and enzyme methods.

*Statistical analysis*

All data were analyzed using SPSS 22.0 statistical analysis software. Measured data were expressed as mean ± standard deviation ($\overline{x}$ ± sd) and compared between groups using independent t-tests. Counted data were expressed as percentages (n/%) and compared using chi-square test. Logistic regression analysis was performed to identify independent risk factors for diabetic foot. Receiver operating characteristic (ROC) curve was plotted to analyze the area under the curve and the optimal cutoff value for each influencing factor, exploring their predictive ability for diabetic foot.

The package "rms" version 4.3 was used to construct a nomogram prediction model for diabetic foot, and the Hosmer-Lemeshow test was carried out to evaluate the goodness of fit of the comprehensive model. Calibration and decision curves were used for internal validation and predictive performance evaluation. A *p*-value of less than 0.05 was considered significant.

## Results

*Comparison of baseline characteristics*

Our results showed significant differences between the diabetic foot group and the non-diabetic foot group in terms of sex, smoking history, duration of diabetes, hyperlipidemia, and atherosclerosis (all P<0.05). However, there were no significant differences in terms of age, body mass index, hypertension, alcohol history, coronary heart disease, and chronic obstructive pulmonary disease between the two groups (all P>0.05). See **Table 1**.

*Comparison of serum marker levels*

There were no significant differences between the two groups in terms of fasting blood glu-

**Table 2.** Comparison of serum marker levels between the two groups

| Item | Diabetic foot group (n=322) | Non-diabetic foot group (n=166) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Fasting blood glucose (mmol/L) | 8.84±3.75 | 8.19±3.38 | 1.875 | 0.061 |
| Glycated hemoglobin (%) | 9.32±2.20 | 7.49±2.45 | 8.371 | 0.000 |
| Alanine aminotransferase (U/L) | 17.34±8.86 | 17.53±8.71 | 0.226 | 0.822 |
| Aspartate aminotransferase (U/L) | 14.55±7.33 | 15.32±8.18 | 1.056 | 0.291 |
| Total bile acid (μmol/L) | 10.34±3.58 | 10.37±2.64 | 0.095 | 0.924 |
| Prealbumin (mg/L) | 253.58±77.79 | 254.20±66.84 | 0.087 | 0.930 |
| Serum total protein (g/L) | 65.38±8.34 | 65.78±7.90 | 0.511 | 0.610 |
| Creatinine (μmol/L) | 136.55±84.67 | 131.82±67.65 | 0.624 | 0.533 |
| Blood urea nitrogen (mmol/L) | 4.92±0.53 | 4.88±0.56 | 0.775 | 0.439 |
| Activated partial thromboplastin time (s) | 29.15±5.93 | 28.78±5.34 | 0.675 | 0.500 |
| Prothrombin time (s) | 12.24±1.23 | 12.28±1.85 | 0.338 | 0.735 |
| Thrombin time (s) | 19.41±2.68 | 19.28±2.67 | 0.508 | 0.611 |
| D-dimer (mg/L) | 0.75±0.51 | 0.83±0.68 | 1.460 | 0.145 |
| C-peptide (ng/mL) | 2.12±1.48 | 2.56±2.41 | 2.491 | 0.013 |

Note: t: data from t-test; $\chi^2$: data from chi-square test.

**Table 3.** Logistic analysis of risk factors for predicting diabetic foot

| Factor | OR | P | 95% CI |
|---|---|---|---|
| Male | 1.780 | 0.003 | 1.011-1.882 |
| Smoking | 1.395 | 0.017 | 1.033-1.906 |
| Duration of diabetes (year) | 3.885 | 0.000 | 1.883-5.377 |
| Glycated hemoglobin (%) | 2.441 | 0.001 | 1.652-4.550 |
| Hyperlipidemia | 1.893 | 0.002 | 1.261-3.344 |
| Atherosclerosis | 2.074 | 0.000 | 1.736-2.193 |

Note: CI: Confidence Interval.

cose, C-peptide, liver function indicators (alanine aminotransferase, aspartate aminotransferase), renal function markers (creatinine, blood urea nitrogen), routine blood indexes, coagulation function markers, and nutritional markers (total bile acid, prealbumin, serum total protein) (all P>0.05). However, there was a significant difference in the glycated hemoglobin level between two groups (P<0.05). See **Table 2**.

*Logistic analysis of risk factors for diabetic foot*

Univariate analysis revealed that the risk factors for diabetic foot included male, smoking history, duration of diabetes, glycated hemoglobin, hyperlipidemia, and atherosclerosis. Subsequently, these factors were considered as independent variables, while the occurrence of diabetic foot was considered as the dependent variable in a Logistic regression model. The results indicated that the above risk factors were independent influencing factors for diabetic foot (all P<0.05). See **Table 3**.

*Construction of nomogram prediction model for diabetic foot through multivariate analysis*

A nomogram prediction model for early warning of diabetic foot associated with type 2 diabetes was constructed using the six independent factors. As shown in the **Figure 2**, in practical application, each point can be determined by drawing a line upwards from the straight line corresponding to each predictive variable on the axis, and the total score can be calculated by summing up the points. By drawing a straight line downwards on the total score axis, the probability of developing diabetic foot associated with type 2 diabetes can be calculated.

*Validation of the nomogram prediction model for diabetes foot*

The findings revealed that the calibration curve of the constructed nomogram prediction model exhibited good consistency. The AUC of the nomogram prediction model was 0.804, with a sensitivity and specificity of 75.3% and 74.4%, respectively. The Harrell's C-index of the predic-

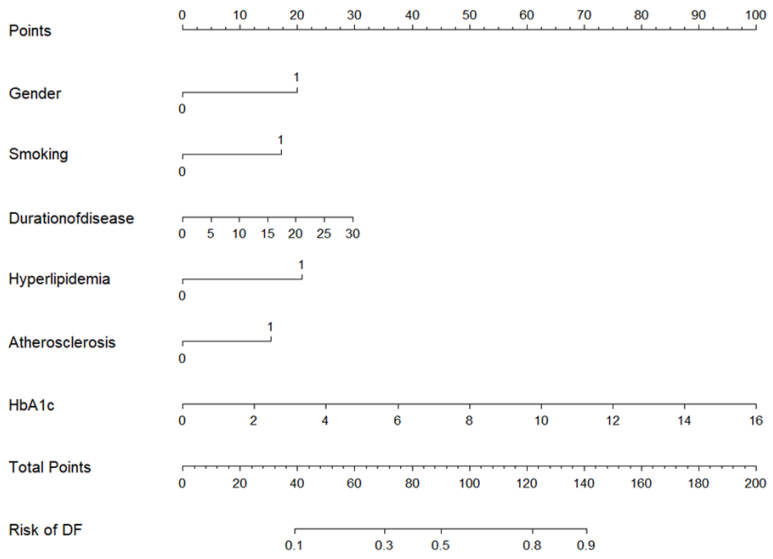


**Figure 2.** A nomogram prediction model for the risk of diabetic foot in diabetes patients. DF: diabetic foot; HbA1c: hemoglobin A1C.

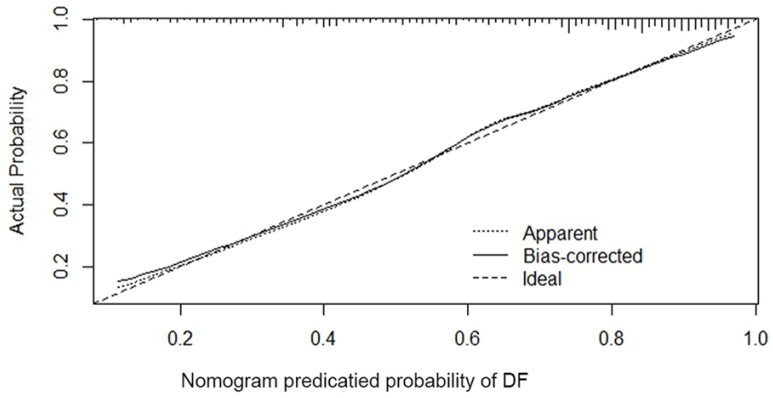


**Figure 3.** Calibration curve of the nomogram model for the risk of diabetic foot in diabetes patients. DF: diabetic foot.

tion model was 0.803 (95% CI: 0.762-0.845), indicating good discriminability of the model. Besides, the decision curve analysis (DCA) showed that the threshold for the nomogram diabetic foot model was >0.675, providing net clinical benefit. See **Figures 3**-**5**.

## Discussion

Diabetic foot is one of the serious complications associated with diabetes, which impacts patients' quality of life and may result in amputation [10, 11]. Research has shown that diabetes-related factors account for over 80% of non-traumatic foot amputations, highlighting diabetes as the most important cause of foot injuries [12]. Furthermore, epidemiological surveys have indicated a prevalence of diabetic foot of nearly 10% in the diabetic population [13]. Therefore, diabetic foot is an important target for intervention in diabetes treatment, and it is of great significance to identify relevant risk factors from baseline data and implement intervention measures to improve the overall diagnosis and treatment of diabetic foot.

In this study, the baseline data of patients with diabetic foot and non-diabetic foot demonstrated that male sex, smoking, duration of diabetes, glycated hemoglobin, hyperlipidemia, and atherosclerosis were independent influencing factors for diabetes foot. Based on these risk factors, a nomogram prediction model for diabetic foot was developed. It showed good predictive performance from the results of ROC and DCA. Application of this model in clinical practice could effectively reduce the incidence of diabetic foot and improve the prognosis of such patients.

Diabetic foot is closely related to male sex. This study revealed a higher proportion of male patients with diabetic foot, which may be attributed to men engaging in physical activities that lead to increased energy consumption. Moreover, men tend to have poorer compliance, resulting in reduced diabetes control rates and subsequently leading to the diabetic foot [14-16]. Smoking has been proven to be closely associated with the occurrence of diabetic foot. Substances presenting in tobacco, when burned at high temperatures, can increase insulin resistance, leading to poor blood glucose control. Furthermore, smoking exacerbates endothelial cell damage, causing endothelial dysfunction and affecting blood flow to the feet [17, 18]. The duration of diabetes is a major risk factor for diabetic foot, primarily due to long-term exposure of endothelial

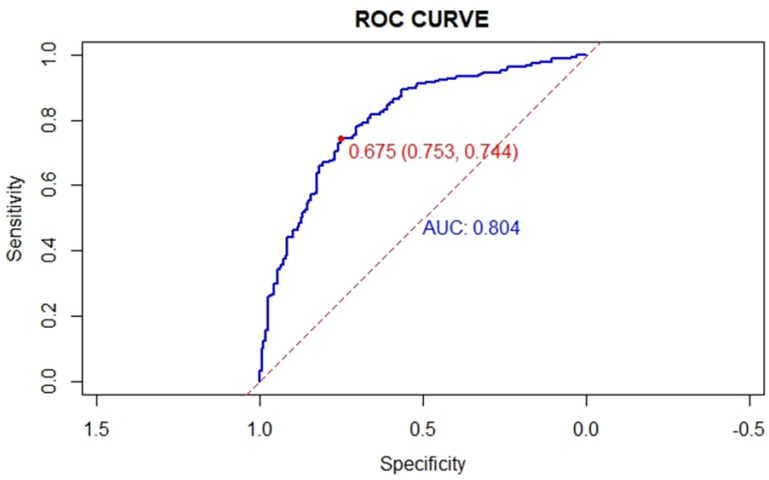


**Figure 4.** ROC curve of the variables associated with diabetic foot in diabetes patients. AUC: area under curve; ROC: receiver operating characteristic.

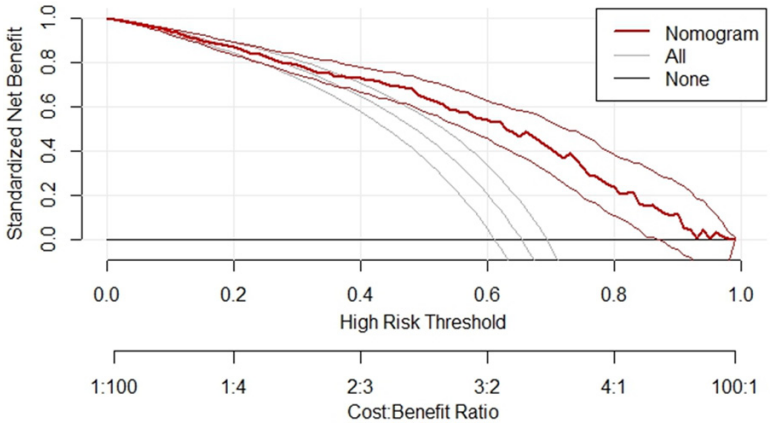


**Figure 5.** Decision curve of the variables associated with diabetic foot in diabetic patients.

cells to a high-glucose environment, reflecting on continuous endothelial damage to the blood vessels in foot and subsequent vascular occlusion and impaired blood flow [19-21]. Glycated hemoglobin reflects blood glucose control over the past three months. If a patient has high levels of glycated hemoglobin, it indicates poor blood glucose control, which in turn activates various pathways such as the polyol pathway, advanced glycation end products, and hexosamine pathway, further exacerbating endothelial cell damage in the lower limb blood vessels and worsening vascular injury [22, 23]. Hyperlipidemia and atherosclerosis are local pathologic changes that occur after vascular damage. Given the small size of foot blood vessels, once atherosclerosis occurs, it can lead to blockage or even occlusion, resulting in ischemia, hypoxia, and subsequently leading to diabetic foot [24, 25]. Hyperlipidemia can further reduce blood flow to the feet by exacerbating vascular atherosclerosis, thereby worsening the condition of diabetic foot [26, 27]. However, the author found that fasting blood glucose and blood cell analysis were not risk factors for diabetic foot, which may be associated with their higher variability and differ from the conclusions of other studies, possibly due to the sample size.

The construction of a nomogram prediction model for diabetic foot in this study helps clinicians effectively assess the patients' condition based on their baseline characteristics. It also facilitates patients and their families in understanding their own condition and the risk of developing diabetic foot, enabling precise intervention measures based on individual characteristics.

Internal validation and clinical prediction performance evaluation further assessed the detection performance of the nomogram model. The results showed that the model for diabetic foot has desirable accuracy and clinical utility. However, this study has certain limitations. First, it is a single-center study, which limits the diversity and generalizability of the included individuals. Further research with larger sample sizes and multiple centers is needed to improve the model. Secondly, the nomogram prediction model has not been externally validated with an independent dataset, which may affect the reliability of the study results and requires further investigation.

Finally, Chinese residents have certain lifestyle habits that vary throughout the year. For instance, during winter, people tend to have longer intervals between showers compared to summer. Moreover, there is an inability to define

prolonged sitting accurately. Therefore, it is not currently feasible to incorporate them into our study. Additionally, the lack of imaging data results in the loss of some predictive functions related to imaging indicators. Therefore, it is necessary to strengthen the provision of clinical data.

In conclusion, this study constructed a nomogram model for predicting diabetic foot in diabetes patients based on factors such as gender, smoking history, duration of diabetes, glycated hemoglobin, hyperlipidemia, and atherosclerosis. The model has good predictive value for diabetic patients with foot complications and has high clinical utility.

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## Disclosure of conflict of interest

None.

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