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ORIGINAL RESEARCH

Construction of a Nomogram-Based Prediction Model for the Risk of Diabetic Kidney Disease in T2DM

Xian Wang[1], Xiaming Liu[1], Jun Zhao[1], Manyu Chen[1], Lidong Wang[2]

[1]Graduate School of Chengde Medical College, Chengde, Hebei, People's Republic of China; [2]Department of Endocrinology and Immunology, Chengde Central Hospital Affiliated to Chengde Medical College, Chengde, Hebei, People's Republic of China

Correspondence: Lidong Wang, Department of Endocrinology and Immunology, Chengde Central Hospital Affiliated to Chengde Medical College, Chengde, Hebei, People's Republic of China, Tel +86 13703142117, Email whlfdjs@126.com

Introduction: To investigate the predictors of diabetic kidney disease (DKD) in type 2 diabetes mellitus (T2DM) patients and establish a nomogram model for predicting the risk of DKD.

Methods: The clinical data of T2DM patients, admitted to the Endocrinology Department of Chengde Central Hospital from October 2019 to September 2020 and divided into a case group or a control group based on whether they had DKD, were collected. The predictive factors of DKD were screened by univariate and multivariate analysis, and a nomogram prediction model was constructed for the risk of DKD in T2DM. Bootstrapping was used for model validation, receiver operating characteristic (ROC) curve and GiViTI calibration curve were used for evaluating the discrimination and calibration of prediction model, and decision analysis curve (DCA) was used for evaluating the practicality of model.

Results: Predictors for DKD are diabetic retinopathy (DR), hypertension, history of gout, smoking history, using insulin, elevation of body mass index (BMI), triglyceride (TG), cystatin C (Cys-C), and reduction of 25 (OH) D. The nomogram prediction model based on the above nine predictors had good representativeness (Bootstrap method: precision: 0.866, Kappa: 0.334), differentiation [the area under curve (AUC) value: 0.868], and accuracy (GiViTI-corrected curved bands, P = 0.836); the DAC curve analysis showed that the prediction model, whose threshold probability was in the range of 0.10 to 0.70, had clinical practical value.

Conclusion: The risk of DKD in T2DM could be predicted accurately by DR, hypertension, history of gout, smoking history, using insulin, elevation of BMI, TG, Cys-C, and reduction of 25 (OH) D.

Keywords: type 2 diabetes mellitus, diabetic kidney disease, predictive model, 25-hydroxyvitamin D, diabetic retinopathy

Introduction

According to the latest epidemiological survey, the overall prevalence rate of type 2 diabetes mellitus (T2DM) in China, whose trend continued to increase had reached 14.92%, and the treatment rate and the standard rate of the diagnosed patients were less than 50%.[1] T2DM can result in many complications, serious harm, high teratogenic and disabling rates, which seriously affects the life and prognosis of patients. The main manifestations of diabetic kidney disease (DKD), whose onset is insidious, are increased foam in urine in the early stage, and gradually hypertension, decreased urine volume, edema and other symptoms, and finally kidney failure.[2] The prevalence rate of DKD in T2DM patients in China was as high as 21.8%, which has become the main cause of chronic kidney disease in China.[3] However, few studies have focused on the risk of DKD in T2DM patients.

The purpose of this study was to investigate the predictors of DKD in T2DM and establish a prediction model based on the clinical data of T2DM patients, so as to identify high-risk patients with DKD early and reduce the risk of DKD.

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Methods

Study Designs and Participants

This was a hospital-based, retrospective study. We selected all the patients with DKD in T2DM admitted to the Second Affiliated Hospital of Chengde Medical College from October 2019 to September 2020. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Chengde Medical College and was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the patients. In total, 403 participants aged 23–81 years were included in the study. Of these patients, 59 (14.6%) were the patients with DKD, 212 (52.6%) were male, and 118 (29.3%) had diabetic retinopathy (DR). The inclusion criteria for patients with DKD were (1) T2DM[4] and (2) age ≥ 18 years old. The exclusion criteria for the study were (1) other types of diabetes, (2) cancer, (3) infection, (4) severe liver dysfunction, (5) chronic renal insufficiency caused by other reasons, (6) the inaccuracy of urinary albumin/creatinine ratio (UACR), and (7) missing data. DKD, in the absence of signs or symptoms of other primary causes of kidney damage, is usually clinically diagnosed based on the presence of albuminuria defined as a urinary albumin-to-creatinine ratio ≥30 mg/g and/or reduced eGFR which was <90 mL/min/1.73m^2. The clinical and demographic characteristics of the study participants are summarized in Table 1.

Table 1 Clinical and Demographic Characteristics of the Study Participants

Variables	Non-DKD (n=344)	DKD (n=59)	*t/U/χ²*	*P*
Gender			9.571	0.002
Male	170 (49.4)	42 (71.2)		
Female	174 (50.6)	17 (28.8)		
Age (years)	56 (51,63)	58 (51,64)	9317.000	0.314
Hypertension			11.464	0.001
Yes	157 (45.6)	41 (69.5)		
No	187 (54.4)	18 (30.5)		
CHD			3.692	0.055
Yes	39 (11.3)	12 (20.3)		
No	305 (88.7)	47 (79.7)		
Stroke			5.445	0.020
Yes	34 (9.9)	12 (20.3)		
No	310 (90.1)	47 (79.7)		
History of gout			13.877	<0.001
Yes	13 (3.8)	10 (16.9)		
No	331 (96.2)	49 (83.1)		
Duration (years)			8961.500	0.109
<1	29 (8.4)	3 (5.1)		
1–10	154 (44.8)	22 (37.3)		
>10	161 (46.8)	34 (57.6)		
Smoking			11.422	0.001
Yes	124 (36.0)	35 (59.3)		
No	220 (64.0)	24 (40.7)		
Drinking			6.881	0.009
Yes	130 (37.8)	33 (55.9)		
No	214 (62.2)	26 (44.1)		
Using insulin			12.419	<0.001
Yes	148 (43.0)	40 (67.8)		
No	196 (57.0)	19 (32.2)		
DPN			1.415	0.234
Yes	268 (77.9)	50 (84.7)		
No	76 (22.1)	9 (15.3)		

(*Continued*)

Table 1 (Continued).

Variables	Non-DKD (n=344)	DKD (n=59)	$t/U/\chi^2$	*P*
DR			7196.000	<0.001
NDR	257 (74.7)	28 (47.5)		
NPDR	85 (24.7)	26 (44.1)		
PDR	2 (0.6)	5 (8.5)		
BMI (kg/m^2)	25.8 (23.8,27.9)	27.0 (25.7,29.4)	7187.500	<0.001
Fatty liver			5.836	0.016
Yes	212 (61.6)	46 (78.0)		
No	132 (38.4)	13 (22.0)		
Visceral fat area (cm^2)	93 (71,119)	112 (85,132)	7698.500	0.003
Glucose random (mmol/L)	12.0 (9.2,14.9)	13.2 (10.4,16.6)	8536.500	0.051
HbA1c/%	9.0±1.9	8.9±1.8	1.298	0.748
FC-P (mmol/L)	1.93 (1.33,2.55)	1.49 (1.18,2.38)	8855.000	0.118
ALT (U/L)	18 (13,27)	12 (16,26)	9157.000	0.230
AST (U/L)	16 (13,21)	15 (11,20)	8773.500	0.096
ALB (g/L)	40.6±4.6	40.2±5.7	2.839	0.574
DBIL (umol/L)	3.3 (2.4,4.3)	2.9 (2.2,3.6)	8429.500	0.038
TBIL (umol/L)	11.2 (8.8,14.5)	10.5 (8.0,12.6)	8765.500	0.094
UREA (mmol/L)	5.7±0.9	11.8±3.8	20.952	0.009
UA (umol/L)	271 (225,328)	310 (223,392)	8290.500	0.025
CR (umol/L)	52 (43,62)	59 (51,77)	6969.500	<0.001
FPG (mmol/L)	7.2 (5.9,9.0)	7.5 (5.8,9.4)	9972.500	0.832
TG (mmol/L)	1.73 (1.21,2.58)	2.52 (1.41,4.40)	7282.000	<0.001
HDL-C (mmol/L)	1.23±0.29	1.21±0.36	0.016	0.686
TC (mmol/L)	4.4 (3.7,5.2)	4.4 (3.4,5.4)	10,112.500	0.966
Cys-C (mg/L)	0.95 (0.86,1.05)	1.05 (0.96,1.21)	6255.000	<0.001
LDL-C (mmol/L)	2.35 (1.82,2.92)	2.09 (1.49,2.71)	8419.500	0.037
PTH (pg/mL)	36.36 (28.95,44.10)	37.93 (25.29,47.92)	10,189.500	0.756
25(OH)D (ng/mL)	14.39 (10.19,18.36)	11.76 (8.22,17.62)	8327.500	0.028
Monocyte (×10^9/L)	0.42±0.31	0.48±0.27	1.995	0.122
Lymphocyte (×10^9/L)	1.96 (1.58,2.42)	2.05 (1.57,2.63)	9661.500	0.556
AIP	0.15 (−0.01,0.34)	0.32 (0.12,0.60)	7161.500	<0.001

Notes: The p values were calculated using Two-sample *t*-test, Chi-square test, Fisher's exact test, or Mann–Whitney *U*-test according to the type of variables.

Abbreviations: DKD, diabetic kidney disease; CHD, coronary heart disease; DPN, diabetes peripheral neuropathy; DR, diabetic retinopathy; NDR, no diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; BMI, body mass index; HbA1c, Hemoglobin A1c; FC-P, fasting C-peptide; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; DBIL, direct bilirubin; TBIL, total bilirubin; UREA, urinary albumin/creatinine ratio; CR, creation; FPG, fasting blood glucose; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; TC, total cholesterol; Cys-C, cystatin C; LDL-C, low density lipoprotein cholesterol; PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D; AIP, atherogenic index of plasma.

Candidate Variables

There were 37 variables classified into three categories in our study, as explanatory risk factors for the patients with DKD. The demographic characteristics included age, sex, history of smoking and drinking, and body mass index (BMI). The clinical information of the patients included duration of T2DM, anamnesis, using insulin after admission, diabetic microangiopathy, fatty liver, and visceral fat area. The history of hypertension disease, coronary heart disease (CHD), stroke, and gout were in the anamnesis. The diabetic microangiopathy contained DKD, diabetes peripheral neuropathy (DPN), and diabetic retinopathy (DR). In addition, 21 blood biochemical indicators which may be helpful in predicting the risk of DKD were included in the study. The complete blood count, liver function test, renal function test, blood fat, fasting plasma glucose (FPG), glucose random, hemoglobin A1c (HbA1c) levels, fasting C-peptide (FC-P), 25-hydroxyvitamin D (25(OH)D), parathyroid hormone (PTH), and atherogenic index of plasma (AIP) which is equal to lg (TG/HDL-C).[5]

The result of weight in kilograms divided by the square of height in meters is the BMI. The history of hypertension disease, CHD, stroke, and gout were definite according to the previous medical history. The presence of DR was diagnosed by two professional ophthalmologists by reading the result of wide-area fundus photography, optical coherence tomography, and fundus fluorescein angiography. The venous blood of the patients was collected at 5 am after an overnight fast of at least 8 h for biochemical tests, except for glucose randomly collected at admission.

Statistical Analysis

Statistical analyses were conducted using SPSS version 26.0 and R version 4.3.1 for Windows. In univariate analysis, the quantitative variables that met normal distribution and variance homogeneity test were expressed as mean ± SD and were compared by the Student's *t*-tests. The other quantitative variables expressed as median [interquartile range (IQR), 25–75%] were compared using the Mann–Whitney *U*-test. Categorial variables compared by the Chi-square tests, continuity correction Chi-square tests, or the Mann–Whitney *U*-test were expressed as number and percentage. The predictive model was established through stepwise logical regression used to filter variables, which were statistical differences in univariate analysis. Evaluate the representativeness of the model through bootstrap (n = 1000), nomogram column graph visualized the model, Receiver Operating Characteristic (ROC) curve evaluated the predictive performance of the model, the GiViTI calibration curve compared the consistency between actual values and model predictions, and the Decision Curve Analysis (DCA) was for the practicality of the model. Bilateral $P \leq 0.05$ was statistically significant.

Results

Clinical and Demographic Characteristics of the Patients

A total of 403 patients in T2DM with DKD met the inclusion criteria in the research. Table 1 summarizes the clinical and demographic characteristics of the patients. Fifty-nine cases (14.6%) of these were the patients with DKD, while the non-DKD group comprised 344 cases (85.4%). Univariate regression analysis showed that the rate of males, history of hypertension, stroke, gout, smoking, and drinking, DR, fatty liver, and using insulin in the DKD group was significantly higher than that in the non-DKD group ($P < 0.05$). The value of BMI, visceral fat area, UREA, uric acid (UA), creatinine (CR), triglyceride (TG), Cys-C, and AIP was also significantly higher in the DKD group ($P < 0.05$). In addition, the direct bilirubin (DBIL), 25(OH)D, and low-density lipoprotein cholesterol (LDL-C) were lower in the DKD group ($P < 0.05$).

Feature Selection

Taking DKD as the dependent variable, variables with statistically significant differences in univariate analysis were taken as independent variables, and the result of feature screening based on logistic regression analysis is shown in Table 2 which included the history of hypertension, gout, and smoking, using insulin, BMI, TG, Cys-C, 25(OH)D, and DR (0 = NDR, 1 = NPDR, 2 = PDR).

The generalized variance inflation factor (GVIF) values of these were 1.047, 1.094, 1.074, 1.076, 1.054, 1.049, 1.031, 1.085, and 1.048, respectively, which did not support multicollinearity.[6]

Construction of a Nomogram-Based Prediction Model

Based on the results of feature selection, a nomogram-based prediction model of DKD in T2DM was constructed. Figure 1 shows a nomogram-based model consisting of scores, predictors, total scores, and occurrence risk. The scale of each line segment represents the value range corresponding to the predictor, and the length of the line segment is the value of the contribution of the predictor to the risk of DKD occurrence. The score at the top of the figure represents the corresponding score of each predictor under different values. The sum of score values of all predictors is calculated based on the score of each predictor, and the predicted value of DKD risk could be obtained on the Risk of DKD axis at the bottom.

Table 2 Feature Selection for DKD

Variables	β	P	OR	95% CI
Using insulin	0.867	0.023	2.380	1.128~5.023
Hypertension	0.830	0.026	2.294	1.106~4.759
History of gout	1.860	0.002	6.421	1.925~21.411
Smoking	1.079	0.003	2.942	1.435~6.030
BMI	0.153	0.010	1.166	1.037~1.310
TG	0.204	0.008	1.226	1.055~1.426
Cys-C	2.644	0.000	14.046	3.356~58.933
25(OH)D	−0.080	0.017	0.923	0.864~0.986
DR		0.000		
NPDR	1.228	0.001	3.413	1.647~7.073
PDR	3.143	0.003	23.177	2.832~189.663
Intercept	−10.321	0.000	0.000	

Abbreviations: DKD, diabetic kidney disease; BMI, body mass index; TG, triglyceride; Cys-C, cystatin C; 25(OH)D, 25-hydroxyvitamin D; DR, diabetic retinopathy; NPDR, non-proliferative diabetic; PDR, proliferative retinopathy.

Model Performance

The representativeness of the model was verified by bootstrapping. The accuracy was 0.866 and the Kappa value was 0.334, indicating that the representativeness of the model was acceptable.

The area under the ROC curve shown in Figure 2 was 0.868 (95% CI: 0.814~0.921). The critical value of the model was 0.178 with the maximum Jorden index (0.642), when the sensitivity was 0.813 and the specificity was 0.828, indicating that the model had good prediction efficiency and differentiation. Figure 3 shows the GiViTI calibration curve of the model, whose 80% and 95% confidence intervals did not cross the 45° diagonal bisector. The P value of it was 0.836, indicating that the calibration curve of the model was close to the actual observation probability. Figure 4 shows the DCA of this model. When the prediction value of the model was between 0.10 and 0.70, it had clinical practical value for predicting the risk of T2DM progression to DKD.

Discussion

In this study, history of hypertension, gout, and smoking, DR, using insulin, BMI, TG, Cys-C, and 25(OH)D were as the feature variables by stepwise Logistic regression to construct a nomogram-based model to predict the risk of DKD in T2DM patients. The model had good representativeness, the ability to predict, high consistency between actual values and predictions, and good practicality by bootstrapping ROC curve, GiViTI calibration curve, and DCA.

In this study, the history of hypertension disease was an independent risk factor for DKD in T2DM, which was consistent with previous research.[7] Actively controlling blood pressure is considered the cornerstone of preventing and treating DKD and the guidelines recommend that the blood pressure control target for DKD is under 130/80mmHg, the preferred drug angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blocker (ARB) drugs.[2] In recent years, it has been found that sodium-glucose cotransporter 2 inhibitor (SGLT2i), dipeptidyl peptidase IV inhibitor (DPP-4i), and glucagon-like peptide-1 receptor agonist (GLP-1RA) have not only hypoglycemic effects, but also antihypertensive effect, and have certain renal benefits for DM,[8–10] which may be related to inhibiting inflammatory response and oxidative stress in T2DM.[11,12] Therefore, the above hypoglycemic drugs should be taken as soon as possible to strengthen the protection of the kidney for T2DM with hypertension.

In this study, univariate analysis found that UA and the history of gout in DKD group were significantly higher than those in non-DKD group, and logistic analysis found that the latter was an independent risk factor for DKD, which was consistent with the conclusions of ROY.[13] The possible reasons are related to hyperuricemia aggravating HOMA-IR, increasing local inflammation and oxidative stress, and aggravating atherosclerosis, leading to kidney injury and renal function decline.[14–16] Therefore, the history of gout may have a certain predictive value for DKD, and clinicians should

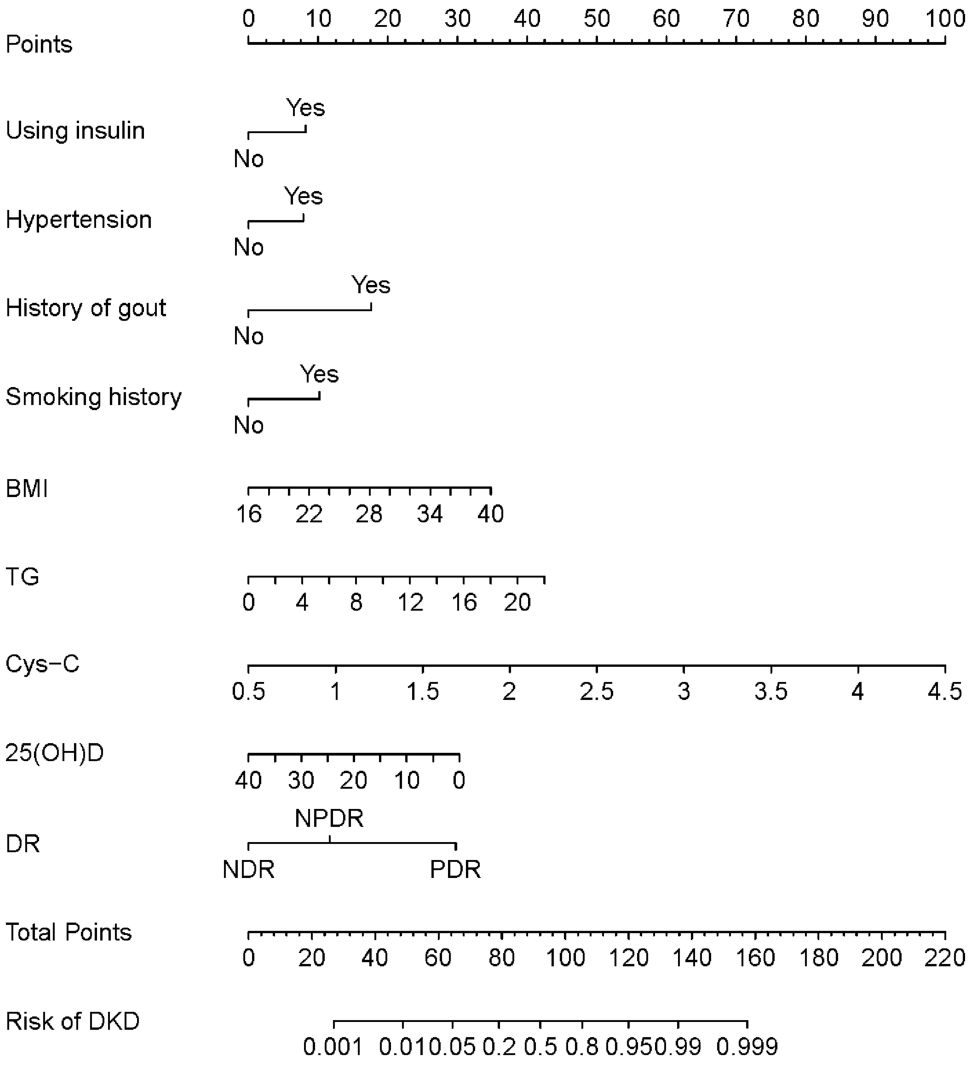

Figure 1 A nomogram predicting the risk of DKD in T2DM.
Abbreviations: BMI, body mass index; TG, triglyceride; Cys-C, cystatin C; 25(OH)D, 25-hydroxyvitamin D; DR, diabetic retinopathy; NDR, no diabetic retinopathy; NPDR, non-proliferative diabetic; PDR, proliferative retinopathy; DKD, diabetic kidney disease; T2DM, type 2 diabetes mellitus.

strengthen the management of blood uric acid in T2DM. For T2DM with a history of gout, attention should be paid not only to the uric acid but also to the changes in renal function and kidney structure.

DR and DKD, the main manifestations of diabetic microvascular complications, have common risk factors such as poor blood glucose control and hypertension, which often coexist in T2DM. Compared with DKD, which needs to be confirmed by kidney biopsy, DR can be diagnosed by fundus photography, so many clinicians often use DR to predict the presence of DKD. Sasso[17] found that urinary albumin excretion rate (AER) may be associated with DR in T2DM with DKD, and this relationship was confirmed in patients with heavier DR. In this study, it was found that DR was correlated with DKD, which was consistent with the above conclusions. In addition, the probability of DKD in NPDR patients was 3.4 times that of NDR patients and the probability of DKD in PDR patients was 23.2 times that of NDR patients in this study. However, a large study[18] in China found there were different risk factors in DR and DKD. The team[18] believed that although DR and DKD have similar pathogenesis, there are still differences in some pathogenesis, so DR cannot be used to judge whether DKD is present. One of the reasons for the above differences may be the heterogeneity of inclusion criteria, exclusion criteria, and experimental design methods.

Animal study[19] has shown that cigarette smoke worsens kidney damage in diabetic rats, and exposure to smoke for 4 weeks worsens DKD progression in diabetic mice. Han[20] found that people who smoked, compared with non-smoking,

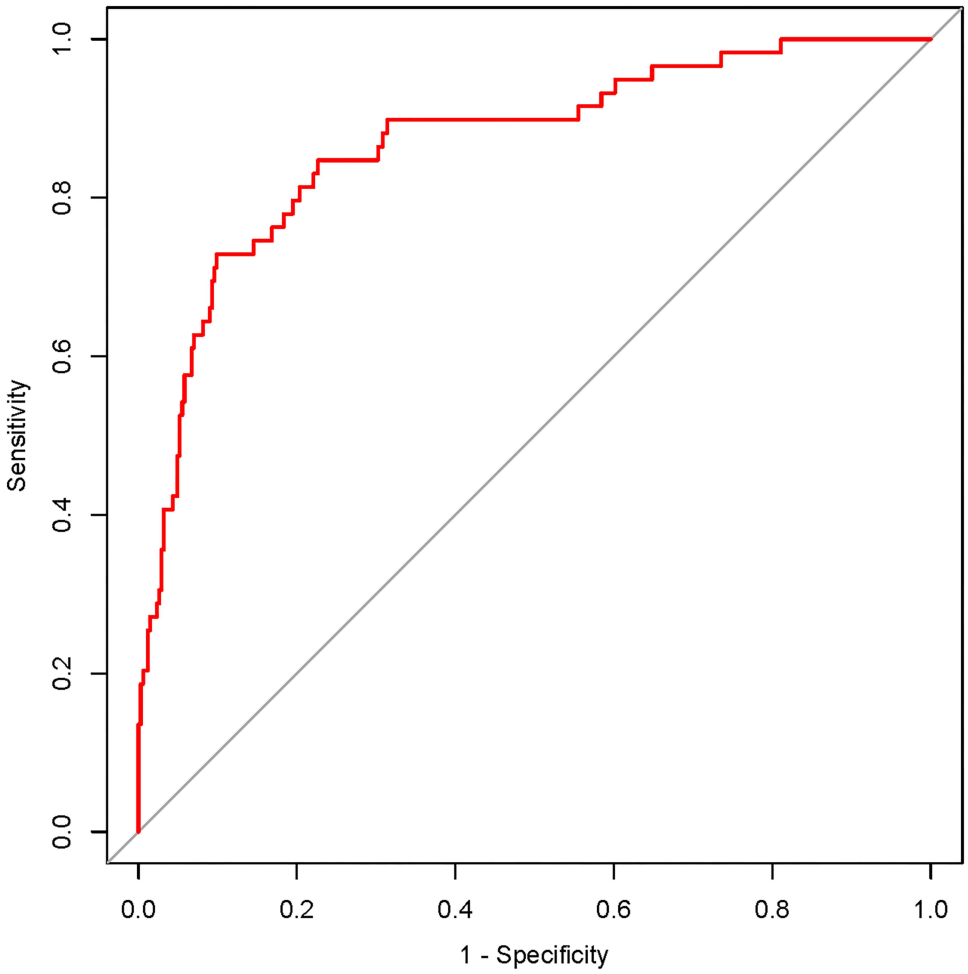

Figure 2 ROC curves basing on the nomogram model predicting the risk of DKD in T2DM.
Abbreviations: ROC, receiver operating characteristic; DKD, diabetic kidney disease; T2DM, type 2 diabetes mellitus.

showed a moderate decrease in glomerular filtration rate (eGFR), accompanied by tubular atrophy and renal interstitial fibrosis. Besides, blood glucose and lipid levels were blood glucose and lipid levels in the smoking.[20] In this study, having a history of smoking was an independent risk factor for DKD in T2DM, and the probability of DKD in T2DM patients with a history of smoking was 3 times that of those without a history of smoking. On the one hand, the harmful components in tobacco may directly damage the intima of blood vessels, reduce the elasticity of blood vessels, promote the infiltration of inflammatory factors and white blood cells into the blood vessel wall, cause vascular constriction, exacerbate blood hypercoagulability, and lead to endothelial dysfunction, thus initiating or aggravating atherosclerosis and affecting the filtration function of the glomeruli.[21] On the other hand, smoking may cause an increase in blood sugar and blood lipid, aggravate the damage of renal tubule and renal interstitial caused by high glucose and high lipid toxicity and oxidative stress, and further promote the occurrence of DKD.[22] Therefore, health education and smoking cessation guidance for T2DM patients are of great significance for the prevention and treatment of DKD.

The use of insulin was a predictor of DKD in this study whose reason may be patients can manage their blood glucose through appropriate exercise, diet control, oral hypoglycemic drugs, and so on in the early stage of onset of T2DM or when the disease is relatively mild. Only when patients cannot reach the blood glucose standard through the above factors will clinicians recommend patients to use insulin to control blood glucose. Additionally, some patients with poor blood sugar control in the above way refuse to use insulin therapy for various reasons until the situation is relatively awful. Therefore, it is not difficult to imagine that patients treated with insulin are poor in β cell, more serious disease, and more diabetes complications, which result in the higher risk in DKD.

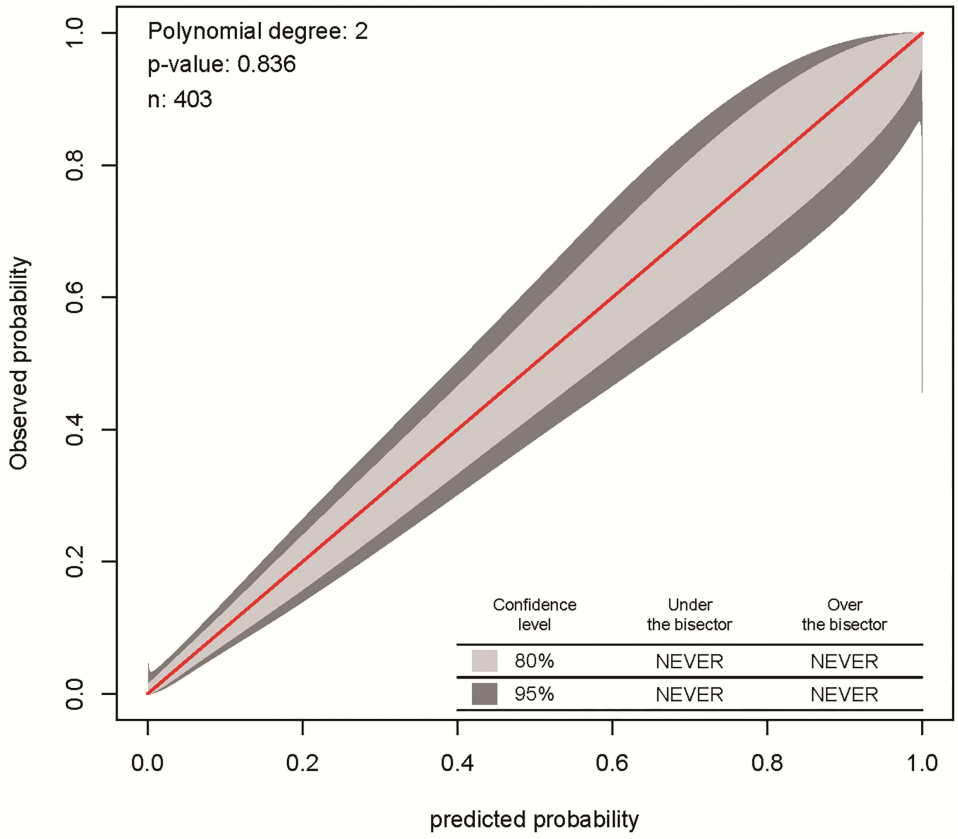

Figure 3 GiViTI calibration curve basing on the nomogram model predicting the risk of DKD in T2DM.
Abbreviations: DKD, diabetic kidney disease; T2DM, type 2 diabetes mellitus.

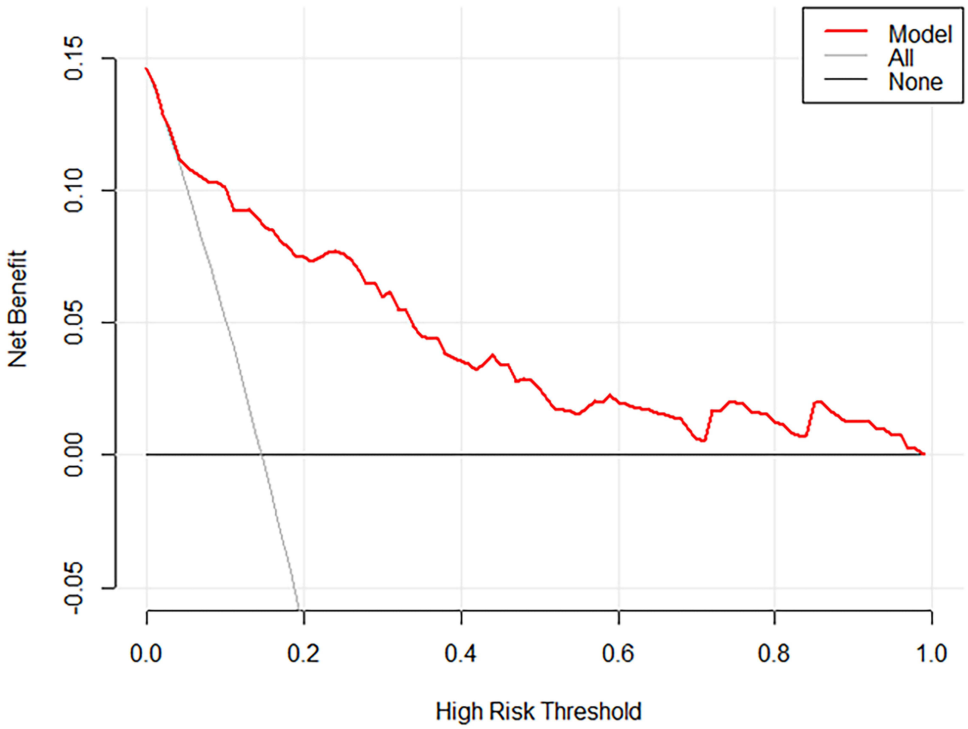

Figure 4 DCA basing on the nomogram model predicting the risk of DKD in T2DM.
Abbreviations: DCA, decision curve analysis; DKD, diabetic kidney disease; T2DM, type 2 diabetes mellitus.

In this study, BMI was the independent risk factor for DKD in T2DM, which was consistent with the conclusions of previous studies.[22–24] In the pathological mechanism, higher BMI may promote the occurrence of DKD through promoting HOMA-IR, chronic inflammatory response, endothelial dysfunction, fibrosis, and thrombosis.[23–26] HOMA-IR, which has a complex relationship with DKD, usually promotes the occurrence of DKD in the early stage and is generally present in end-stage DKD through various mechanisms.[27] There are many high-affinity insulin receptors in renal tubule cells and podocytes. When HOMA-IR is present, the glomerular insulin signal is impaired, causing renal epithelial cell dysfunction, proteinuria, and promoting renal fibrosis.[28] Hence, HOMA-IR may be an important pathological component of DKD. Because higher BMI is often accompanied by HOMA-IR, patients with T2DM should keep BMI within an appropriate range to reduce the HOMA-IR, which may prevent the occurrence of DKD to a certain extent.[26]

Dyslipidemia, one of the main causes of kidney injury, plays an important role in the occurrence and development of DKD.[29] Our study found that TG was one of the predictors for DKD, consistent with the conclusion of previous studies.[30] The studies[31,34] found that at least eight standard predictors, such as eGFR, urinary albumin, SCR, T1DM disease course, HbA1c, age, and BMI, effectively indicated that Cys-C, renal resistance index, and renal injury molecular-1 may be related to the risk of DKD, which confirmed the potential value of Cys-C in predicting the risk of developing DKD in patients with T1DM. The results of this study showed that patients with higher Cys-C had a significantly increased risk of DKD, and subsequent analyses found that Cys-C could be used to predict the occurrence of DKD. However, the specificity of Cys-C is poor, which is a shortcoming of Cys-C.

Renal fibrosis is one of the markers of progression of DKD, and epithelial-mesenchymal-transition (EMT) is a key mechanism of progression of diabetic renal fibrosis.[35,36] In animal study, the lack of Vit D can promote the occurrence of EMT and lead to the rapid progression of DKD by enhancing the expression of transcriptional co-suppressor ZEB1/ZEB2 and down-regulating the expression of miR-200b gene, which could inhibit the transcription and translation of ZEB1/ZEB2.[37] In this study, 25(OH)D was found to be a protective factor for the progression of T2DM to DKD, which was consistent with previous studies.[38,39] The prevalence of DKD is still increasing despite the use of Vit D replacement therapies, based mainly on blood glucose, and blood pressure control to delay the progression of ESRD. However, it is indisputable that correcting Vit D can still play a role in delaying the development of DKD.[40,41]

We should acknowledge several limitations of this study. First, this was a single-center retrospective study, which inevitably had a certain selection bias. Second, some confounding factors not included in the study may not have been adequately addressed. Third, the sample size of this study was not large enough, and external verification was absent. In the future, multi-center prospective and large sample studies can be further conducted to verify our results and improve the robustness and extrapolation of the model's prediction efficiency.

Conclusion

The prediction model constructed in this study had 9 predictors, including history of hypertension disease, gout, smoking, insulin use, BMI, DR, TG, Cys-C, and 25(OH)D, and had a good overall performance after the tests, bootstrapping, ROC curve, GiViTI calibration curve, and DCA.

What is more, the nomogram-based model can help clinicians to predict the risk of DKD in a non-invasive and accurate way, in order to facilitate early action, which may have significant benefits for patients.

Consent for Publication

Consent for publication was obtained from all the authors.

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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 declare that they have no conflicts of interest in relation to this work.

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