ORIGINAL RESEARCH

Development of Serum Lactate Level-Based Nomograms for Predicting Diabetic Kidney Disease in Type 2 Diabetes Mellitus Patients

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Purpose: To establish nomograms integrating serum lactate levels and traditional risk factors for predicting diabetic kidney disease (DKD) in type 2 diabetes mellitus (T2DM) patients.

Patients and methods: A total of 570 T2DM patients and 100 healthy subjects were enrolled. T2DM patients were categorized into normal and high lactate groups. Univariate and multivariate logistic regression analyses were employed to identify independent predictors for DKD. Then, nomograms for predicting DKD were established, and the model performance was evaluated using the area under the receiver operating characteristic curve (AUC), calibration, and decision curve analysis (DCA).

Results: T2DM patients exhibited higher lactate levels compared to those in healthy subjects. Glucose, platelet, uric acid, creatinine, and hypertension were independent factors for DKD in T2DM patients with normal lactate levels, while diabetes duration, creatinine, total cholesterol, and hypertension were indicators in high lactate levels group ($P<0.05$). The AUC values were 0.834 (95% CI, 0.776 to 0.891) and 0.741 (95% CI, 0.688 to 0.795) for nomograms in both normal lactate and high lactate groups, respectively. The calibration curve demonstrated excellent agreement of fit. Furthermore, the DCA revealed that the threshold probability and highest Net Yield were 17–99% and 0.36, and 24–99% and 0.24 for the models in normal lactate and high lactate groups, respectively.

Conclusion: The serum lactate level-based nomogram models, combined with traditional risk factors, offer an effective tool for predicting DKD probability in T2DM patients. This approach holds promise for early risk assessment and tailored intervention strategies.

Keywords: serum lactate, diabetic kidney disease, nomograms, prediction model, risk factors

Introduction

Diabetic kidney disease represents a significant and severe microvascular complication of diabetes mellitus (DM), which is characterized by elevated urine protein and reduced glomerular filtration rate (GFR).[1,2] With a global estimate of around 537 million adult diabetic patients in 2021 released by the International Diabetes Federation (IDF).[3] It is concerning that approximately 20–40% of diabetic patients will develop DKD, which stands as a contributor to chronic

kidney disease and end-stage kidney disease (ESKD).[4,5] Advanced patients need dialysis or kidney transplantation to maintain life, greatly elevating the risk of cardiovascular morbidity and mortality.[6] Particularly, patients experiencing albuminuria and reduced GFR of DKD have greater risk for mortality (HR: 2.08, 95% CI: 1.88–2.30).[7] Thus, there is a pressing need for enhanced predictive tools and markers to identify and manage DKD in its early stage.

While DKD diagnosis is established through criteria set by organizations such as the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) (2007)[8] and Kidney Disease: Improving Global Outcomes (KDIGO) (2022) guidelines,[9] which incorporate estimated glomerular filtration rate (eGFR), urine albumin-to-creatinine ratio (UACR), and renal biopsy, which is the gold standard. While it is important to recognize the variability and fluctuations in GFR and UACR in diabetes patients over time, the evidence suggests a decrease in albuminuria prevalence with time and a reduced eGFR increased, indicating non-classical courses of DKD including non-albuminuric DKD.[4] Current management strategies for DKD encompass lifestyle modifications, self-management practices, first-line drug therapies like metformin and sodium-glucose cotransporter-2 inhibitors (SGLT2i), as well as additional risk factors control.[9] However, the risk for ESKD increased in T2DM (HR: 2.32, 95% CI 2.30–2.35) and in type 1 diabetes mellitus (T1DM) (HR: 10.92, 95% CI 10.15–11.75) for a failure to achieve target levels of these risk factors.[10] Therefore, measurements of eGFR and UACR commonly used to predict progression to the advanced stages of DKD are proving inadequate. It has become imperative to develop more novel effective predictive tools to accurately gauge the progression of DKD.

Current studies have shown that advanced age, prolonged diabetes duration, and elevated blood pressure, lipids, body mass index (BMI), and glycosylated hemoglobin are risk factors for DKD.[10,11] With the development of metabolomics, more and more biomarkers of DKD have been explored.[12,13] Lactate, a metabolite associated with glucose metabolism and energy supply under anaerobic conditions, has recently gained attention for its potential role as a biomarker. It is becoming increasingly clear that lactate, previously considered a metabolic waste, is also involved in cell signaling, gene expression, and disease occurrence.[14] Multiple biological processes are involved in the occurrence of DKD, especially the glycolytic pathway, confirming that lactate is one of the most important biomarkers for non-invasive early diagnosis of DKD.[15] Therefore, evaluating the level of lactate in patients with T2DM, and exploring the prediction of DKD risk from the perspective of lactate levels may provide a new direction for the diagnosis and treatment of DKD.

Nomogram is a method to quantitatively evaluate whether multiple variables are involved in the occurrence of a certain disease, which displays the functional relationship between multiple variables in plane coordinates, draws multiple line segments at a specific proportion according to the regression results, and visualizes the results of the regression equation, so that the individual's disease risk or survival probability can be easily calculated.[16] Previous studies have shown the application of nomogram in DKD,[17,18] but did not separately explain the risk factors of DKD under different lactate levels and the establishment of prediction models. To address the need for more accurate prediction models, this study sought to assess serum lactate levels in healthy individuals and T2DM patients. We explored the high-risk factors of DKD, and established risk prediction models for DKD based on serum lactate levels, employing the nomogram technique. It provides a simple, low-cost, and highly sensitive tool for the prediction of DKD, and provides new ideas for the clinical diagnosis and treatment of DKD.

Methods
Study Design and Participant Characteristics

This retrospective study collected data from patients with T2DM admitted to the Department of Endocrinology and Metabolism of the Affiliated Hospital of Southwest Medical University and healthy subjects (no history of disease and abnormal physical examination) from the physical examination center between September 2018 and March 2023. The study cohort consisted of 100 healthy individuals, and a total of 570 patients among the 1100 patients with T2DM, including 305 males (53.5%), and 248 patients with DKD among diabetes patients, as per criteria established by WHO,[19] NKF-KDOQI (2007),[8] and (KDIGO) (2022) guidelines,[9] DKD was diagnosed as eGFR <60 mL/min/1.73m^2 and/or UACR >30 mg/g for ≥3 months caused by diabetes. Hyperlactatemia is defined as the serum lactate level greater than 2.5 mmol/L, without acute infection, surgery, trauma, and other stressful situations. Inclusion criteria:

patients over 18 years old diagnosed with T2DM. Exclusion criteria: patients with severe visceral diseases, recent acute complications of diabetes, recent infection, chronic infectious diseases, pregnancy, malignant tumors, renal function damage caused by other clearly diagnosed renal diseases, acute renal injury, patients with lactic acidosis, unwilling collaborator. All protocols followed the ethical guidelines of Declaration of Helsinki, the study has been approved by the Ethics Committee of the Affiliated Hospital of Southwest Medical University (license number: KY2023142). When we retrospectively collected the data of previous cases, written informed consent was waived due to the retrospective nature and low risk of the study. We obtained informed consent when collecting blood and urine from healthy people.

Data Collection and Clinical Variables

Patient data encompassed hospitalization number, sex, age, duration of diabetes, anthropometric data of height (cm), body weight (BW, Kg), systolic blood pressure (SBP, mmHg), diastolic blood pressure (DBP, mmHg), heart rate (HR, bpm), lifestyle habits (smoking, drinking), comorbidities, and hypoglycemic drug use, BMI was calculated as weight $(kg)/(height (m))^2$. Blood cell composition (white blood cell count (WBC, 10^9/L), neutrophil cell rate (NEU-R, %), lymphocyte rate (LYM-R, %), monocyte rate (MONO-R, %), red blood cell count (RBC, 10^{12}/L), hemoglobin (HGB, g/L), platelet count (PLT, 10^9/L)), biochemical analyses (Liver function (alanine aminotransferase (ALT, U/L), aspartate aminotransferase (AST, U/L)), renal function (urea (mmol/L), uric acid (UA, μmol/L), creatinine (Crea, μmol/L)), fasting blood glucose (FBG, mmol/L) and blood lipid profile (total cholesterol (TC, mmol/L), triglyceride (TG, mmol/L), high-density lipoprotein cholesterol (HDL-C, mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L))) were performed using automatic hematology analyzer (sysmex18932) and automatic biochemical analyzer (Mindray BS-2000M). Blood glucose, lactate (mmol/L), albumin in urine (ALBU, mg/L), and creatinine were measured by hexokinase method, lactate oxidase method, immune transmission turbidimetric method, and sarcosine oxidase method, respectively. EGFR (mL/min) is calculated using the CKD-EPI formula.

Establishment of Prediction Model and Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics 19 and R software (R version 4.2.1). Normality of data distribution was assessed using the Shapiro–Wilk test. Descriptive statistics included mean ± standard for normal distribution continuous variables, median (95% confidence interval (CI)) for non-normal distribution variables, and n (%) for categorical variables. The differences between groups of continuous variables were evaluated by Student's *t*-test, while categorical variables were assessed with chi-square test. According to the concentrations of lactate in serum, patients with T2DM were categorized into normal lactate (≤2.5 mmol/L, n = 202) and high lactate (>2.5 mmol/L, n = 368) groups. Univariate and multivariate logistic regression analyses were employed using the R language *rms* package to identify DKD risk factors for each lactate group. With optimal predictive factors selected, the features were considered to be odds ratios (OR) and a *P* value with 95% CI, the statistical significance levels were all two-sided. Furthermore, we developed DKD prediction models using independent risk factors identified from the multivariate logistic regression analysis using the R language *rms* package. For the normal lactate level group, DKD linear_predictors = 0.106 * glucose + 0.007 * PLT + 0.005 * UA + 0.023 * Crea + 1.048 (hypertension yes) – 6.871. Similarly, for the high lactate level group, DKD linear_predictors = 0.065 * duration + 0.019 * Crea + 0.304 * TC + 0.830 (hypertension yes) – 4.269. DKD predicted_probability = $\frac{1}{1 + e^{-linear\_predictor}}$. These formulas were used to develop nomograms for individualized risk assessment. The discrimination and prediction ability of the models were assessed using the C-index called area under the receiver operating characteristic (ROC) curve (AUC) operated by R language *pROC* package. The consistency between predicted results and observed results was evaluated using the Hosmer–Lemeshow goodness-of-fit test and calibration curve (operated by R language *rms* package). We utilized the R language's *nricens* package to perform DCA for assessing the clinical applicability of the nomograms. Using the probability threshold as the X-axis and the net benefit as the Y-axis, DCA evaluated the utility of the nomograms across different thresholds. This analysis aided in determining the effectiveness of the nomograms in guiding clinical decision-making.

Results

Participant Characteristics

A total of 570 patients with T2DM and 100 healthy subjects participated in the study. Of the patients with T2DM, 322 were diagnosed as T2DM without DKD (176 males and 146 females), and 248 were diagnosed with DKD (129 males and 119 females) by physicians, resulting in a DKD prevalence of 43.5%. Patients with T2DM exhibited higher age, BW, BMI, SBP, DBP, glucose levels, lactate levels, TG, Urea, UA, Crea, ALBU, UACR, ALT, AST, WBC, NEU-R, MONO-R, and lower levels of HR, HDL-C, eGFR, LYM-R, PLT compared with healthy controls, with statistically significant differences (Supplement Table 1). Notably, serum lactate levels were higher in T2DM patients compared to healthy subjects, with average concentrations of 2.48 mmol/L in healthy subjects, 2.93 mmol/L in T2DM patients without DKD, and 2.84 mmol/L in T2DM patients with DKD (Figure 1).

Participant Stratification and Risk Factors

Based on serum lactate levels, all patients with T2DM were categorized into two groups: a normal lactate group and a high lactate group. Each group of patients was divided into T2DM patients with DKD and those without. Analysis of the differences between DKD and T2DM patients without DKD within the normal and high lactate groups was summarized (Tables 1 and 2). In the normal lactate group, patients with DKD exhibited a longer duration of diabetes, higher levels of glucose, WBC, NEU-R, PLT, Urea, UA, Crea, TG, ALBU, UACR, and a higher prevalence of hypertension as well as insulin therapy, but the levels of LYM-R, RBC, and HGB were lower than patients without DKD ($P < 0.05$). Among T2DM patients with hyperlactatemia, compared with patients without DKD, DKD patients were older, had a longer duration of diabetes, higher levels of Urea, Crea, TC, LDL-C, ALBU, and UACR, lower levels of RBC, HGB, along with a higher prevalence of hypertension and insulin therapy ($P < 0.05$). Univariate logistic analysis revealed that duration of diabetes, levels of glucose, WBC, NEU-R, LYM-R, HGB, PLT, Urea, UA, Crea, TG, and comorbid conditions such as hypertension, cerebral infarction, and insulin therapy were influencing factors of DKD in T2DM patients with normal lactate level. Among T2DM patients with hyperlactatemia, significant influencing factors for DKD included age, duration of diabetes, levels of Urea, LYM-R, MONO-R, RBC, HGB, Urea, Crea, TC, LDL-C, and comorbid conditions such as hypertension, fatty liver, and insulin therapy. Variables with $P < 0.1$ in univariate logistic regression analysis were considered independent variables, and multivariate logistic regression analysis identified glucose, PLT, UA, Crea, and hypertension as independent risk factors for DKD in the normal lactate group. In the
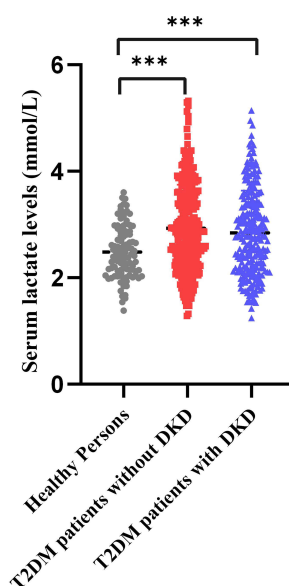

Figure 1 Serum lactate levels in subjects with healthy persons, T2DM patients without DKD, and DKD patients. Serum lactate levels were higher in T2DM patients with DKD and those without than in healthy controls. ***p<0.001.

Table 1 Baseline Characteristics of T2DM Patients Without or with DKD with Normal Levels of Serum Lactate

Characteristics	T2DM Patients Without DKD	DKD	P value
n	108	94	
Gender, n (%)			0.922
Female	59 (54.6%)	52 (55.3%)	
Male	49 (45.4%)	42 (44.7%)	
Age (Years), median (IQR)	61 (54.75, 69)	62.5 (53, 70.75)	0.689
Drinking, n (%)			0.738
No	77 (71.3%)	69 (73.4%)	
Yes	31 (28.7%)	25 (26.6%)	
Smoking, n (%)			0.493
No	87 (80.6%)	72 (76.6%)	
Yes	21 (19.4%)	22 (23.4%)	
Durations (years), median (IQR)	10 (4.75, 13.25)	10 (5.25, 17.75)	**0.041**
Glucose (mmol/L), median (IQR)	9.775 (7.235, 13.968)	12.84 (8.8925, 16.383)	**0.002**
BMI (Kg/m^2), median (IQR)	24 (21.775, 26.05)	25.05 (22.825, 26.35)	0.074
WBC (*10^9/L), mean ± sd	5.9508 ± 1.4019	6.6804 ± 1.4077	**< 0.001**
NEU-R (%), mean ± sd	62.924 ± 7.6565	66.328 ± 8.0726	**0.002**
LYM-R (%), mean ± sd	28.091 ± 6.852	24.607 ± 7.2737	**< 0.001**
MONO-R (%), median (IQR)	5.9 (5, 7.1)	5.8 (5.2, 6.975)	0.787
RBC (*10^12/L), median (IQR)	4.4 (4.1, 4.7)	4.2 (3.7, 4.675)	**0.010**
HGB (g/L), median (IQR)	135 (123, 145.25)	125.5 (110, 141.5)	**0.001**
PLT (*10^9/L), median (IQR)	190.5 (153, 221.75)	202.5 (172, 234.75)	**0.026**
ALT (U/L), median (IQR)	20.1 (15.875, 26.425)	19.2 (13.05, 26.05)	0.141
AST (U/L), median (IQR)	20.95 (17.725, 24.625)	19.3 (15.625, 24.75)	0.070
Urea (mmol/L), median (IQR)	5.8 (4.875, 6.8)	7.45 (6.3, 9.6)	**< 0.001**
UA (μmol/L), mean ± sd	298.34 ± 75.323	371.33 ± 108.52	**< 0.001**
Crea (μmol/L), median (IQR)	59.35 (48.925, 69.15)	81.7 (67.35, 122.58)	**< 0.001**
TC (mmol/L), median (IQR)	4.4 (3.7, 5.2)	4.55 (3.7, 5.6)	0.405
TG (mmol/L), median (IQR)	1.4 (1, 1.8)	1.7 (1.125, 2.475)	**0.014**
HDL-C (mmol/L), median (IQR)	1.2 (1, 1.4)	1.1 (0.9, 1.3)	0.119
LDL-C (mmol/L), median (IQR)	2.7 (2, 3.5)	2.7 (1.825, 3.6)	0.798
ALBU (mg/L), median (IQR)	8.15 (4.95, 14.9)	211.45 (44.45, 954.1)	**< 0.001**
UACR (mg/gcr), median (IQR)	10.3 (6.975, 15.75)	278.95 (69, 1623.3)	**< 0.001**
Hypertension, n (%)			**< 0.001**
No	59 (54.6%)	19 (20.2%)	
Yes	49 (45.4%)	75 (79.8%)	
CAD, n (%)			0.061
No	88 (81.5%)	66 (70.2%)	
Yes	20 (18.5%)	28 (29.8%)	
Fatty liver, n (%)			0.445
No	68 (63%)	64 (68.1%)	
Yes	40 (37%)	30 (31.9%)	
Cerebral infarction, n (%)			**0.008**
No	84 (77.8%)	57 (60.6%)	
Yes	24 (22.2%)	37 (39.4%)	
Biguanides, n (%)			0.129
No	42 (38.9%)	27 (28.7%)	
Yes	66 (61.1%)	67 (71.3%)	

Table 1 (Continued).

Characteristics	T2DM Patients Without DKD	DKD	P value
Sulfonylureas, n (%)			0.144
No	64 (59.3%)	65 (69.1%)	
Yes	44 (40.7%)	29 (30.9%)	
Glinides, n (%)			1.000
No	105 (97.2%)	92 (97.9%)	
Yes	3 (2.8%)	2 (2.1%)	
TZDs, n (%)			0.162
No	98 (90.7%)	90 (95.7%)	
Yes	10 (9.3%)	4 (4.3%)	
AGIs, n (%)			0.419
No	86 (79.6%)	79 (84%)	
Yes	22 (20.4%)	15 (16%)	
SGLT2 Inhibitors, n (%)			0.417
No	101 (93.5%)	85 (90.4%)	
Yes	7 (6.5%)	9 (9.6%)	
DPP-IV Inhibitors, n (%)			0.772
No	100 (92.6%)	86 (91.5%)	
Yes	8 (7.4%)	8 (8.5%)	
GLP-1 receptor agonists, n (%)			0.417
No	108 (100%)	92 (97.9%)	
Yes	0 (0%)	2 (2.1%)	
Insulin, n (%)			**0.003**
No	63 (58.3%)	35 (37.2%)	
Yes	45 (41.7%)	59 (62.8%)	

Notes: Normal distribution continuous variables were described by mean ± standard, non-normal distribution continuous variables were described by mean (95% confidence interval (CI)), and categorical variables were expressed as n (%). Bold values indicate statistical significance (p<0.05).
Abbreviations: T2DM, type 2 diabetes mellitus; DKD, diabetic kidney disease; BMI, body mass index; WBC, white blood cell count; NEU-R, neutrophil cell rate; LYM-R, lymphocyte rate; MONO-R, monocyte rate; RBC, red blood cell count; HGB, hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; UA, uric acid; Crea, creatinine; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; ALBU, albumin in urine; UACR, urine albumin-to-creatinine ratio; CAD, coronary artery disease; TZDs, thiazolidinediones; AGIs, α-glucosidase inhibitor; SGLT2 Inhibitors, sodium-glucose cotransporter-2 inhibitors; DPP-IV Inhibitors, dipeptidyl peptidase-IV inhibitors; GLP-1 receptor agonists, glucagon-like peptide-1(GLP-1) receptor agonists.

Table 2 Baseline Characteristics of T2DM Patients Without or with DKD with High Levels of Serum Lactate

Characteristics	T2DM patients without DKD	DKD	P value
n	214	154	
Gender, n (%)			0.584
Female	87 (40.7%)	67 (43.5%)	
Male	127 (59.3%)	87 (56.5%)	
Age (Years), median (IQR)	59 (52.25, 69)	63 (54.25, 71.75)	**0.043**
Drinking, n (%)			0.257
No	138 (64.5%)	108 (70.1%)	
Yes	76 (35.5%)	46 (29.9%)	
Smoking, n (%)			0.989
No	153 (71.5%)	110 (71.4%)	
Yes	61 (28.5%)	44 (28.6%)	

(*Continued*)

Table 2 (Continued).

Characteristics	T2DM patients without DKD	DKD	P value
Durations (years), median (IQR)	7 (3, 10)	10 (6, 19.75)	**< 0.001**
Glucose (mmol/L), median (IQR)	12.42 (8.4675, 18.14)	12.735 (9.65, 17.695)	0.835
BMI (Kg/m^2), median (IQR)	25.05 (22.825, 27.075)	24.9 (22.575, 26.8)	0.717
WBC (*10^9/L), median (IQR)	6.4 (5.425, 7.8)	6.6 (5.8, 7.8)	0.210
NEU-R (%), mean ± sd	63.842 ± 8.3044	64.66 ± 8.9465	0.367
LYM-R (%), mean ± sd	27.495 ± 7.6708	25.942 ± 8.1603	0.063
MONO-R (%), median (IQR)	5.6 (4.8, 6.8)	6.1 (4.9, 7)	0.068
RBC (*10^12/L), mean ± sd	4.7103 ± 0.55865	4.4623 ± 0.62839	**< 0.001**
HGB (g/L), mean ± sd	141.69 ± 16.642	133.8 ± 19.282	**< 0.001**
PLT (*10^9/L), median (IQR)	206 (168, 240.5)	199.5 (167, 243.75)	0.698
ALT (U/L), median (IQR)	20.25 (15.725, 30.375)	20.7 (15.525, 32.275)	0.737
AST (U/L), median (IQR)	19.15 (16.25, 25.175)	20.7 (16.025, 27.125)	0.302
Urea (mmol/L), median (IQR)	5.9 (4.825, 7.275)	6.6 (5.3, 8.275)	**0.004**
UA (μmol/L), mean ± sd	330.68 ± 85.058	344.62 ± 94.65	0.140
Crea (μmol/L), median (IQR)	63.7 (52.425, 74.775)	70.4 (57.75, 93.9)	**< 0.001**
TC (mmol/L), median (IQR)	4.25 (3.6, 5)	4.7 (4.1, 5.4)	**< 0.001**
TG (mmol/L), median (IQR)	1.6 (1.2, 2.675)	1.8 (1.225, 2.975)	0.227
HDL-C (mmol/L), median (IQR)	1.1 (0.9, 1.3)	1.1 (0.9, 1.3)	0.431
LDL-C (mmol/L), median (IQR)	2.5 (1.925, 3.1)	2.85 (2.1, 3.4)	**0.008**
ALBU (mg/L), median (IQR)	10.8 (6.425, 17)	89.25 (43.075, 350.65)	**< 0.001**
UACR (mg/gcr), median (IQR)	11.95 (7.3, 18.2)	132.6 (53.375, 505.38)	**< 0.001**
Hypertension, n (%)			**< 0.001**
No	107 (50%)	39 (25.3%)	
Yes	107 (50%)	115 (74.7%)	
CAD, n (%)			0.108
No	182 (85%)	121 (78.6%)	
Yes	32 (15%)	33 (21.4%)	
Fatty liver, n (%)			0.055
No	109 (50.9%)	94 (61%)	
Yes	105 (49.1%)	60 (39%)	
Cerebral infarction, n (%)			0.128
No	160 (74.8%)	104 (67.5%)	
Yes	54 (25.2%)	50 (32.5%)	
Biguanides, n (%)			0.952
No	52 (24.3%)	37 (24%)	
Yes	162 (75.7%)	117 (76%)	
Sulfonylureas, n (%)			0.599
No	135 (63.1%)	93 (60.4%)	
Yes	79 (36.9%)	61 (39.6%)	
Glinides, n (%)			0.990
No	207 (96.7%)	149 (96.8%)	
Yes	7 (3.3%)	5 (3.2%)	
TZDs, n (%)			0.352
No	196 (91.6%)	145 (94.2%)	
Yes	18 (8.4%)	9 (5.8%)	
AGIs, n (%)			0.838
No	162 (75.7%)	118 (76.6%)	
Yes	52 (24.3%)	36 (23.4%)	
SGLT2 Inhibitors, n (%)			0.179
No	192 (89.7%)	131 (85.1%)	
Yes	22 (10.3%)	23 (14.9%)	

(*Continued*)

Table 2 (Continued).

Characteristics	T2DM patients without DKD	DKD	P value
DPP-IV Inhibitors, n (%)			0.312
No	197 (92.1%)	137 (89%)	
Yes	17 (7.9%)	17 (11%)	
GLP-1 receptor agonists, n (%)			0.453
No	202 (94.4%)	148 (96.1%)	
Yes	12 (5.6%)	6 (3.9%)	
Insulin, n (%)			**0.010**
No	129 (60.3%)	72 (46.8%)	
Yes	85 (39.7%)	82 (53.2%)	

Notes: Normal distribution continuous variables were described by mean ± standard, non-normal distribution continuous variables were described by mean (95% confidence interval (CI)), and categorical variables were expressed as n (%). Bold values indicate statistical significance (p<0.05).
Abbreviations: T2DM, type 2 diabetes mellitus; DKD, diabetic kidney disease; BMI, body mass index; WBC, white blood cell count; NEU-R, neutrophil cell rate; LYM-R, lymphocyte rate; MONO-R, monocyte rate; RBC, red blood cell count; HGB, hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; UA, uric acid; Crea, creatinine; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; ALBU, albumin in urine; UACR, urine albumin-to-creatinine ratio; CAD, coronary artery disease; TZDs, thiazolidinediones; AGIs, α-glucosidase inhibitor; SGLT2 Inhibitors, sodium-glucose cotransporter-2 inhibitors; DPP-IV Inhibitors, dipeptidyl peptidase-IV inhibitors; GLP-1 receptor agonists, glucagon-like peptide-1(GLP-1) receptor agonists.

high lactate group, duration of diabetes, Crea, TC, and hypertension were determined to be independent risk factors for DKD (Tables 3 and 4).

Predictive Nomogram Models

The five variables of glucose, PLT, UA, Crea, and hypertension were integrated into the predictive model for DKD risk in T2DM patients with normal lactate levels. Similarly, duration of diabetes, Crea, TC, and hypertension were included in

Table 3 Univariate and Multivariate Logistic Regression Analysis of DKD Risk in T2DM Patients with Normal Levels of Serum Lactate

Characteristics	Total(N)	Univariate Analysis		Multivariate Analysis	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Gender	202				
Female	111	Reference			
Male	91	0.973 (0.558–1.695)	0.922		
Age (Years)	202	1.010 (0.985–1.037)	0.431		
Drinking	202				
No	146	Reference			
Yes	56	0.900 (0.485–1.671)	0.739		
Smoking	202				
No	159	Reference			
Yes	43	1.266 (0.645–2.485)	0.493		
Durations (years)	202	**1.045 (1.003–1.088)**	**0.034**	1.004 (0.946–1.063)	0.889
Glucose (mmol/L)	202	**1.076 (1.023–1.132)**	**0.004**	**1.108 (1.039–1.177)**	**0.003**
BMI (Kg/m²)	202	1.059 (0.983–1.141)	0.129		
WBC (*10^9/L)	202	**1.452 (1.176–1.792)**	**< 0.001**	1.180 (0.894–1.466)	0.258
NEU-R (%)	202	**1.057 (1.019–1.097)**	**0.003**	1.063 (0.919–1.206)	0.406
LYM-R (%)	202	**0.931 (0.893–0.971)**	**< 0.001**	1.039 (0.881–1.198)	0.633
MONO-R (%)	202	0.977 (0.840–1.137)	0.764		

(*Continued*)

Table 3 (Continued).

Characteristics	Total(N)	Univariate Analysis		Multivariate Analysis	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
RBC (*10^12/L)	202	1.019 (0.921–1.128)	0.715		
HGB (g/L)	202	**0.972 (0.957–0.987)**	**< 0.001**	0.981 (0.958–1.003)	0.087
PLT (*10^9/L)	202	**1.006 (1.001–1.011)**	**0.017**	**1.007 (1.000–1.004)**	**0.017**
ALT (U/L)	202	0.983 (0.957–1.011)	0.233		
AST (U/L)	202	0.969 (0.933–1.008)	0.116		
Urea (mmol/L)	202	**1.566 (1.315–1.866)**	**< 0.001**	1.195 (0.938–1.452)	0.173
UA (μmol/L)	202	**1.009 (1.005–1.012)**	**< 0.001**	**1.020 (1.005–1.040)**	**0.030**
Crea (μmol/L)	202	**1.037 (1.021–1.053)**	**< 0.001**	**1.022 (1.007–1.037)**	**0.006**
TC (mmol/L)	202	1.167 (0.947–1.437)	0.148		
TG (mmol/L)	202	**1.260 (0.976–1.627)**	**0.076**	1.040 (0.805–1.276)	0.742
HDL-C (mmol/L)	202	0.557 (0.245–1.266)	0.162		
LDL-C (mmol/L)	202	1.089 (0.842–1.407)	0.516		
Hypertension	202				
No	78	Reference		Reference	
Yes	124	**4.753 (2.531–8.924)**	**< 0.001**	**2.658 (1.831–3.485)**	**0.020**
CAD	202				
No	154	Reference		Reference	
Yes	48	**1.867 (0.968–3.599)**	**0.062**	0.545 (−0.441–1.532)	0.228
Fatty liver	202				
No	132	Reference			
Yes	70	0.797 (0.445–1.428)	0.446		
Cerebral infarction	202				
No	141	Reference		Reference	
Yes	61	**2.272 (1.230–4.198)**	**0.009**	1.919 (0.885–4.160)	0.099
Biguanides	202				
No	69	Reference			
Yes	133	1.579 (0.874–2.852)	0.130		
Sulfonylureas	202				
No	129	Reference			
Yes	73	0.649 (0.363–1.162)	0.145		
Glinides	202				
No	197	Reference			
Yes	5	0.761 (0.124–4.653)	0.767		
TZDs	202				
No	188	Reference			
Yes	14	0.436 (0.132–1.438)	0.173		
AGIs	202				
No	165	Reference			
Yes	37	0.742 (0.360–1.531)	0.420		
SGLT2 Inhibitors	202				
No	186	Reference			
Yes	16	1.528 (0.546–4.275)	0.420		
DPP-IV Inhibitors	202				
No	186	Reference			
Yes	16	1.163 (0.419–3.229)	0.772		
GLP-1 receptor agonists	202				
No	200	Reference			
Yes	2	6,759,171.6178 (0.000 - Inf)	0.988		
Insulin	202				

(*Continued*)

Table 3 (Continued).

Characteristics	Total(N)	Univariate Analysis		Multivariate Analysis	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
No	98	Reference		Reference	
Yes	104	**2.360 (1.339–4.160)**	**0.003**	1.153 (0.344–1.962)	0.730

Notes: Univariate and multivariate odds ratios (ORs) and 95% confidence intervals (CIs) from univariate and multivariate logistic regression models were applied in the analysis. Bold font indicated p < 0.1 of univariate logistic regression analysis, bold font indicated p < 0.05 of multivariate logistic regression analysis.
Abbreviations: BMI, body mass index; WBC, white blood cell count; NEU-R, neutrophil cell rate; LYM-R, lymphocyte rate; MONO-R, monocyte rate; RBC, red blood cell count; HGB, hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; UA, uric acid; Crea, creatinine; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; CAD, coronary artery disease; TZDs, thiazolidinediones; AGIs, α-glucosidase inhibitor; SGLT2 Inhibitors, sodium-glucose cotransporter-2 inhibitors; DPP-IV Inhibitors, dipeptidyl peptidase-IV inhibitors; GLP-1 receptor agonists, glucagon-like peptide-1(GLP-1) receptor agonists.

Table 4 Univariate and Multivariate Logistic Regression Analysis of DKD Risk in T2DM Patients with High Levels of Serum Lactate

Characteristics	Total(N)	Univariate Analysis		Multivariate Analysis	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Gender	368				
Female	154	Reference			
Male	214	0.890 (0.585–1.353)	0.584		
Age (Years)	368	**1.019 (1.000–1.038)**	**0.044**	0.985 (0.962–1.008)	0.207
Drinking	368				
No	246	Reference			
Yes	122	0.773 (0.496–1.206)	0.257		
Smoking	368				
No	263	Reference			
Yes	105	1.003 (0.634–1.587)	0.989		
Durations (years)	368	**1.084 (1.050–1.119)**	**< 0.001**	**1.069 (1.025–1.114)**	**0.002**
Glucose (mmol/L)	368	0.998 (0.970–1.027)	0.900		
BMI (Kg/m^2)	368	0.999 (0.939–1.062)	0.967		
WBC (*10^9/L)	368	1.069 (0.951–1.202)	0.263		
NEU-R (%)	368	1.011 (0.987–1.036)	0.366		
LYM-R (%)	368	**0.975 (0.949–1.001)**	**0.064**	1.000 (0.969–1.032)	0.999
MONO-R (%)	368	**1.117 (0.995–1.253)**	**0.061**	1.049 (0.911–1.207)	0.508
RBC (*10^12/L)	368	**0.484 (0.334–0.702)**	**< 0.001**	0.774 (0.406–1.479)	0.439
HGB (g/L)	368	**0.975 (0.964–0.987)**	**< 0.001**	0.985 (0.964–1.006)	0.156
PLT (*10^9/L)	368	1.000 (0.997–1.003)	0.879		
ALT (U/L)	368	1.003 (0.990–1.016)	0.689		
AST (U/L)	368	1.009 (0.986–1.033)	0.441		
Urea (mmol/L)	368	**1.181 (1.070–1.303)**	**< 0.001**	0.985 (0.864–1.123)	0.825
UA (μmol/L)	368	1.002 (0.999–1.004)	0.141		
Crea (μmol/L)	368	**1.024 (1.014–1.034)**	**< 0.001**	**1.020 (1.008–1.033)**	**0.001**
TC (mmol/L)	368	**1.264 (1.055–1.515)**	**0.011**	**1.345 (1.107–1.640)**	**0.003**
TG (mmol/L)	368	1.000 (0.905–1.104)	0.998		
HDL-C (mmol/L)	368	1.747 (0.887–3.443)	0.107		
LDL-C (mmol/L)	368	**1.347 (1.073–1.692)**	**0.010**	1.343 (0.942–1.915)	0.103
Hypertension	368				
No	146	Reference		Reference	
Yes	222	**2.949 (1.878–4.631)**	**< 0.001**	**2.570 (1.529–4.318)**	**< 0.001**
CAD	368				

(*Continued*)

Table 4 (Continued).

Characteristics	Total(N)	Univariate Analysis		Multivariate Analysis	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
No	303	Reference			
Yes	65	1.551 (0.906–2.656)	0.110		
Fatty liver	368				
No	203	Reference		Reference	
Yes	165	**0.663 (0.435–1.009)**	**0.055**	0.793 (0.485–1.296)	0.355
Cerebral infarction	368				
No	264	Reference			
Yes	104	1.425 (0.902–2.250)	0.129		
Biguanides	368				
No	89	Reference			
Yes	279	1.015 (0.626–1.647)	0.952		
Sulfonylureas	368				
No	228	Reference			
Yes	140	1.121 (0.732–1.716)	0.599		
Glinides	368				
No	356	Reference			
Yes	12	0.992 (0.309–3.187)	0.990		
TZDs	368				
No	341	Reference			
Yes	27	0.676 (0.295–1.548)	0.354		
AGIs	368				
No	280	Reference			
Yes	88	0.950 (0.584–1.546)	0.838		
SGLT2 Inhibitors	368				
No	323	Reference			
Yes	45	1.532 (0.820–2.863)	0.181		
DPP-IV Inhibitors	368				
No	334	Reference			
Yes	34	1.438 (0.709–2.915)	0.314		
GLP-1 receptor agonists	368				
No	350	Reference			
Yes	18	0.682 (0.250–1.860)	0.455		
Insulin	368				
No	201	Reference		Reference	
Yes	167	**1.728 (1.137–2.627)**	**0.010**	1.091 (0.648–1.838)	0.742

Notes: Univariate and multivariate odds ratios (ORs) and 95% confidence intervals (CIs) from univariate and multivariate logistic regression models were applied in the analysis. Bold font indicated p < 0.1 of univariate logistic regression analysis, bold font indicated p < 0.05 of multivariate logistic regression analysis.
Abbreviations: BMI, body mass index; WBC, white blood cell count; NEU-R, neutrophil cell rate; LYM-R, lymphocyte rate; MONO-R, monocyte rate; RBC, red blood cell count; HGB, hemoglobin; PLT, platelet count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; UA, uric acid; Crea, creatinine; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; CAD, coronary artery disease; TZDs, thiazolidinediones; AGIs, α-glucosidase inhibitor; SGLT2 Inhibitors, sodium-glucose cotranspor-ter-2 inhibitors; DPP-IV Inhibitors, dipeptidyl peptidase-IV inhibitors; GLP-1 receptor agonists, glucagon-like peptide-1(GLP-1) receptor agonists.

the predictive model for DKD risk in T2DM patients with high lactate levels. Multivariate logistic regression analysis of these variables was illustrated in the forest plot (Figure 2), and the features were described by OR and a *P* value with 95% CI. Using the R language to establish nomogram models, which were developed to quantitatively predict the probability of DKD occurrence in T2DM patients with normal levels of lactate (Figure 3A) and high levels of lactate (Figure 3B). According to the degree of influence of each independent variable in the nomogram on the outcome of DKD, we scored the different levels of each variable, corresponding to the scores on the points in the figure, and then
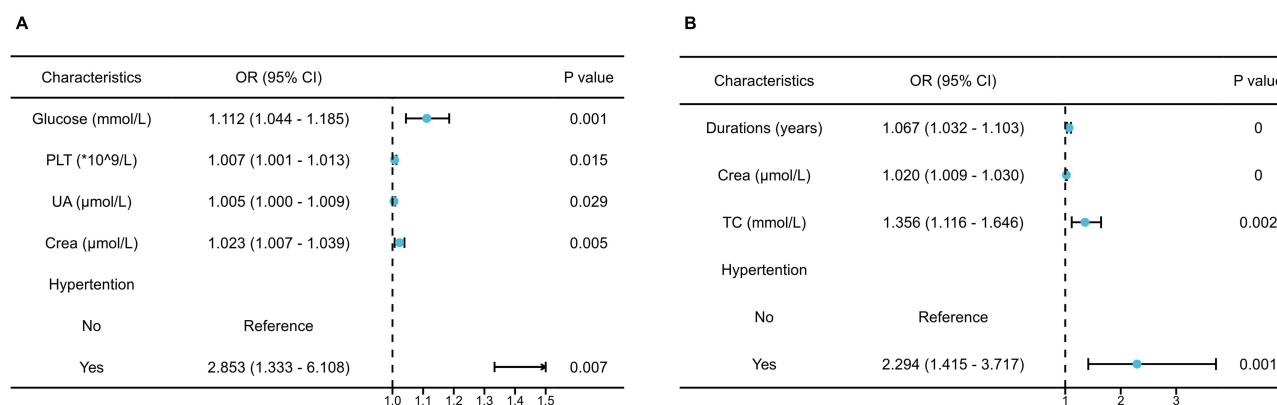
Figure 2 The forest plots of predictors of DKD in T2DM patients classified by lactate levels. The OR and a *p* value with 95% CI of the selected risk factors for DKD risk in T2DM patients with normal (**A**) and high (**B**) serum lactate levels are shown.
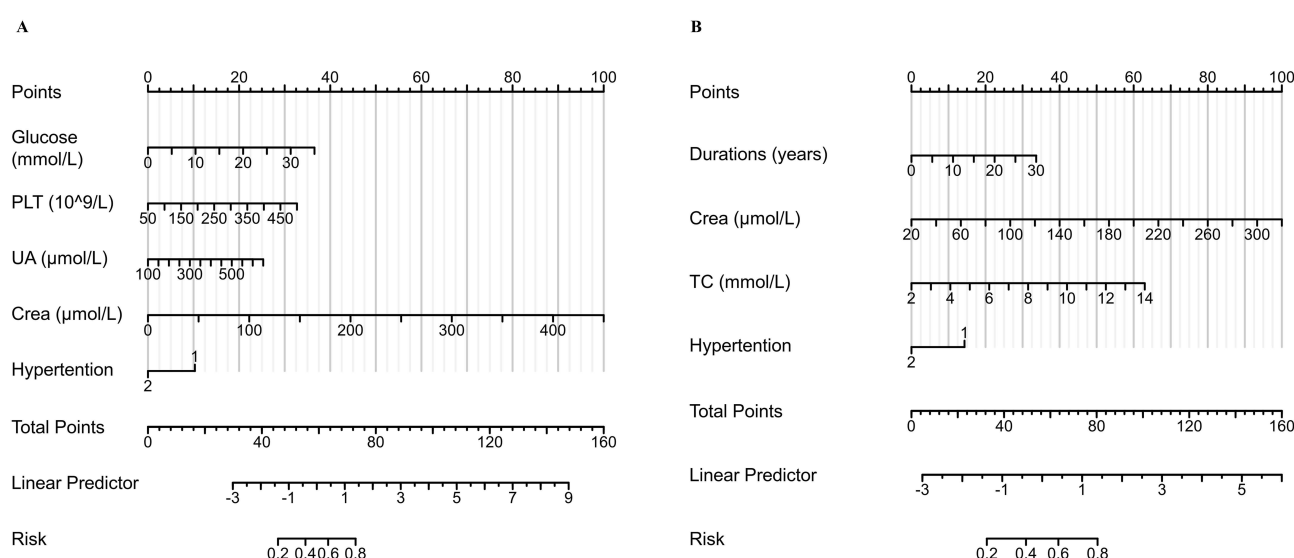

Figure 3 The nomograms to quantitatively predict probability of DKD in T2DM patients classified by lactate levels. (**A**): the nomogram for DKD prediction in T2DM patients with normal lactate levels. (**B**): the nomogram for DKD prediction in T2DM patients with high lactate levels. Each variable's influence is quantified by assigning scores, which are then summed to calculate the total score, the score corresponds to the value on the linear predictor, so as to provides the probability of DKD.

added the scores of each variable to obtain the total score. The score corresponds to the value on the linear predictor, so as to calculate the probability of DKD occurrence. For instance, in the normal lactate group, a T2DM patient with glucose levels of 13.2 mmol/L, PLT of 205 * 10^9/L, UA of 273 μmol/L, Crea of 61.8 μmol/L, and comorbid hypertension, would have an estimated DKD probability of 44.3%. Similarly, in the high lactate group, a patient with T2DM with a diabetes duration of 10 years, Crea of 91.8 μmol/L, TC of 3.6 mmol/L, and comorbid hypertension, would have an estimated DKD probability of 52.0%.

Prediction Model Performance

The C-index was utilized to assess the discrimination and performance of the prediction models. The ROC curves of different DKD risk prediction models for T2DM patients with normal and high lactate levels were depicted (Figure 4A and B, respectively). The AUC for DKD risk screening models in both normal lactate and high lactate groups indicated good discrimination, with values of 0.834 (95% CI, 0.776 to 0.891) and 0.741 (95% CI, 0.688 to 0.795), respectively. Sensitivity and specificity values were 0.691 and 0.870, 0.597 and 0.804 for normal lactate and high lactate groups, respectively. The calibration of the models was evaluated using the Hosmer–Lemeshow goodness-of-fit test and
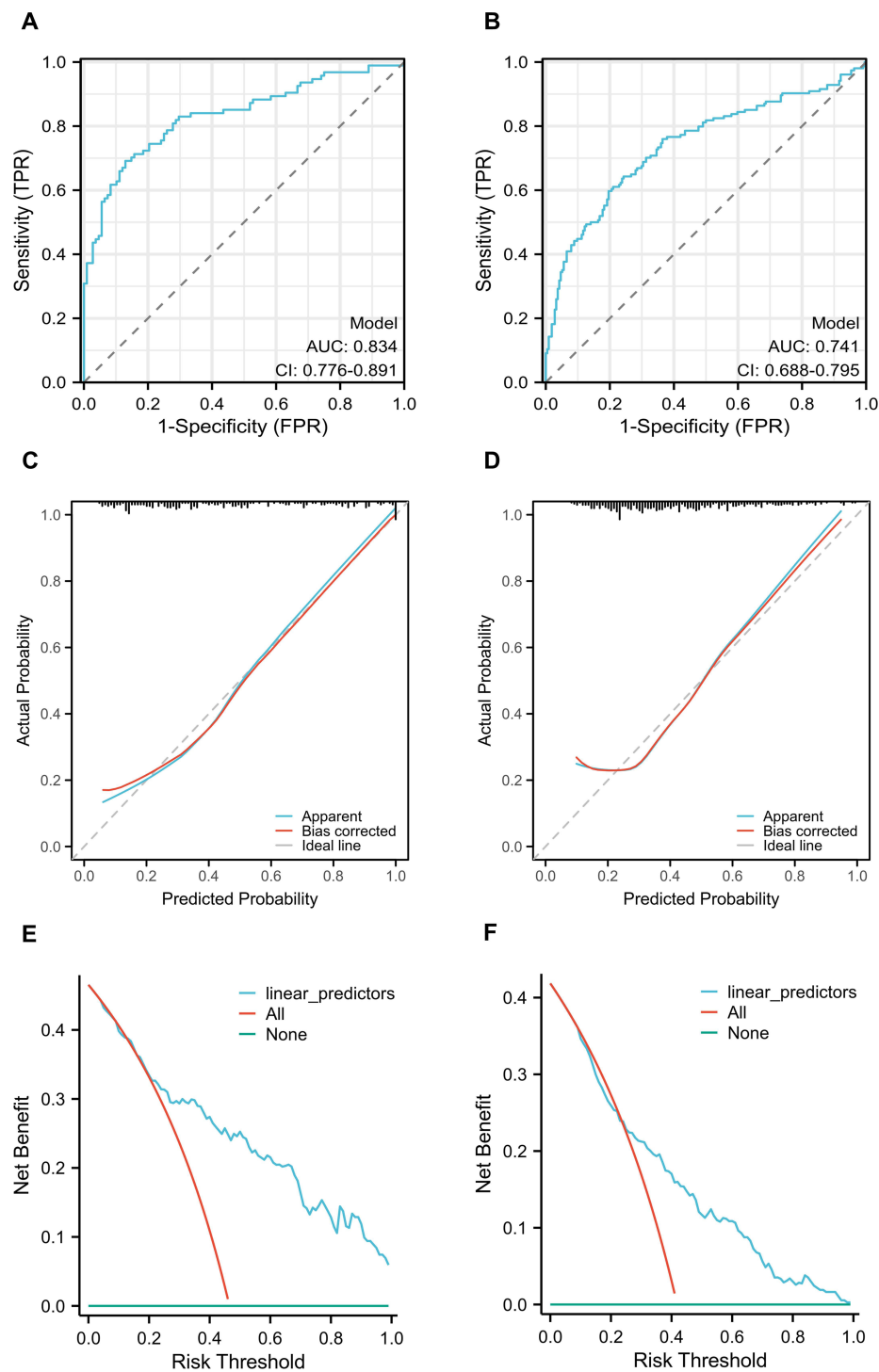
Figure 4 The performance of predictive models for DKD in T2DM patients classified by lactate levels. (**A**): ROC curves of DKD prediction model in T2DM patients with normal lactate levels. (**B**): ROC curves of DKD prediction model in T2DM patients with high lactate levels. The y-axis and x-axis represent the true and false-positive rate of the risk prediction, respectively. The blue line represents the performance of the nomogram of DKD risk in patients with T2DM with normal (**A**) and high (**B**) levels of serum lactate. (**C**): calibration curves of DKD prediction model in T2DM patients with normal lactate levels. (**D**): calibration curves of DKD prediction model in T2DM patients with high lactate levels. The y-axis represents actual diagnosed cases of DKD, the x-axis represents the predicted risk of DKD. The diagonal dotted line represents a perfect prediction by an ideal model, the red line represents the performance of the nomogram, of which a closer fit to the diagonal dotted line represents a better prediction. (**E**): the DCA of DKD prediction model in T2DM patients with normal lactate levels. (**F**): the DCA of DKD prediction model in T2DM patients with high lactate levels. The y-axis measures the net benefit and the x-axis measures the risk threshold. The blue line represents the DKD incidence risk nomogram. The red line represents the assumption that all patients are diagnosed as DKD. The green line represents the assumption that no patients are diagnosed as DKD. The DCA showed that if the threshold probability of a patient is from 17 to 99% in T2DM patients with normal levels of serum lactate and from 24 to 99% in high levels of serum lactate, using the nomogram to predict DKD incidence risk adds more benefit than the diagnosing-all-patients scheme.

calibration curve, showing excellent agreement between the predicted and actual DKD risk in both normal group (χ^2 = 3.4565, P = 0.9025) and high lactate group (χ^2 = 14.723, P = 0.0648). The calibration curve for the nomogram models to predict DKD risk demonstrated a robust degree of fit in normal lactate and high lactate group (Figure 4C and D, respectively). Furthermore, the DCA revealed that the threshold probability and highest net yield for the models in normal lactate and high lactate groups were 17–99% and 0.36, and 24–99% and 0.24, respectively (Figure 4E and F), which suggested that the DKD risk prediction models could provide more beneficial outcomes than the diagnosing-all-patients scheme within this threshold probability range.

Discussion

Despite ongoing research, the pathogenesis of DKD remains incompletely understood, and current treatments have limitations.[20–22] Standard clinical markers like eGFR and UACR commonly reflect the advanced stages of DKD, because albuminuria was reported to follow a remission/regression trajectory, and eGFR decline was insufficient to predict disease progression in the early stages.[4] Consequently, early non-invasive and straightforward screening is crucial for the prevention and treatment of DKD. Better markers and predictive tools are needed for early diagnosis of DKD. A nomogram, a visual representation of a prediction model, intuitively depicts the prediction probability of outcomes by calculating the functional relationship between multiple variables.[16] In the present study, we analyzed the clinical data of T2DM patients using univariate and multivariate logistic regression analyses. Our findings revealed that glucose, PLT, UA, Crea, and hypertension were independent factors for DKD in T2DM patients with normal lactate levels, while duration of diabetes, Crea, TC, and hypertension were indicators in high lactate levels group. We constructed a DKD risk evaluation model, aiding clinicians in making individualized diagnosis and treatment of DKD at the earliest stages on various factors and lactate levels in T2DM patients. The ROC, calibration, and DCA curves demonstrated favorable model performance.

Traditional factors such as longer duration of T2DM, hypertension, and metabolic perturbations (eg, chronic hyperglycemia, hyperuricemia, high triglyceride levels) are well-known risk factors for DKD occurrence.[23,24] With the advent of metabolomics, different metabolic substrates and products are detected, facilitating the identification of key biomarkers characterizing metabolic diseases.[25,26] Consequently, new biomarkers aiding in the diagnosis and evaluation of therapeutic effects of DKD have been widely developed.[27] Enrichment analyses confirmed the involvement of several biological pathways in DKD pathogenesis, such as the urea cycle, tricarboxylic acid cycle, glycolysis, and amino acid metabolisms.[13,28,29] Higher level of lactate, a metabolite produced under anaerobic conditions during the glycolysis for energy, has been observed in T2DM and DKD patients.[14,30,31] Similarly, in the present study, we found that serum lactate levels were higher in T2DM patients with DKD and those without than in healthy controls. Previously, a meta-analysis indicated that increased lactic acid in urine and kidney tissue served as an early diagnostic biomarker for DKD.[15] Studies have confirmed that long-term hyperglycemia and mitochondrial damage in DKD patients led to increased oxygen demand and relative hypoxia in the kidneys, enhancing glycolysis and increasing lactate production.[32,33] The pathogenesis of DKD was linked to renal lactate dehydrogenase A (LDHA)-mediated lactic acidosis, which led to fibrosis and mitochondrial abnormalities.[34] The condition of DKD patients was improved when LDHA was used as a therapeutic target.[31,35] However, serum lactate levels in DKD patients are higher than those in healthy controls, which may be affected by the use of drugs, like ARB drugs.[31] This suggests the necessity for larger sample and multicenter studies to detect serum lactate levels, while also paying attention to the effects of drugs on lactate metabolism.

Several studies have identified hyperglycemia, serum uric acid (SUA), and platelets as risk factors for DKD in DM patients, associating them with increased risk of microalbuminuria, rapid eGFR decline, and progression to end-stage renal disease (ESRD).[36–39] Our findings in the normal lactate level group corroborated these observations, demonstrating significantly higher blood glucose, SUA, and platelet levels of DKD patients compared to those in T2DM patients without DKD, establishing them as independent risk factors for DKD. Current studies have suggested that hyperglycemia triggers oxidative stress and inflammation through activation of signaling pathways such as NF-κB, PI3K/Akt, and MAPK/ERK, ultimately contributing to DKD pathogenesis.[40] Hyperuricemia was postulated to induce and promote renal fibrosis via activation of the transforming growth factor-β 1/Smad2/3 pathway.[41] Platelet activation, characterized by pro-inflammatory factor secretion, platelet–leukocyte interaction, and pro-fibrotic responses, was thought to exacerbate renal

function decline.[42] Conversely, interventions like intensive glucose control, SUA levels reduction, and antiplatelet therapy have demonstrated efficacy in improving renal function, reducing UACR, and slowing DKD progression.[42–44] Collectively, these findings underscore the critical role of managing hyperglycemia, SUA levels, and platelet activity in both DKD prevention and treatment strategies.

Risk factors associated with DKD in T2DM patients with elevated lactate levels were identified in the present study, which included diabetes duration, total cholesterol, creatinine, and hypertension, while these findings corroborate existing literature.[23,45–47] Emerging evidence suggested potential links: A study found that the media fold change of urinary lactate and creatinine revealed a trend corresponding to stages of DKD and gradually increased.[48] DM patients with longer durations (>20 years) exhibited higher LDH levels compared to those with shorter durations (<5 years).[49] Furthermore, DKD patients with elevated LDH displayed worse renal function (lower eGFR, higher creatinine and ACR), more severe pathology, and a higher risk of ESRD progression.[50] Obese adolescents with higher D-lactate levels also had higher total cholesterol/HDL-C ratios, supporting a potential link between lactate and lipid metabolism.[51] Similar observations were made in DKD patients, where higher LDH levels correlated with elevated total cholesterol.[50] Increased serum lactate in high-fat and high-cholesterol (HFHC) fed monkeys served as a potential predictor for impaired glucose tolerance and insulin resistance, suggesting its possible role in prediabetic states.[52] Higher lactate quartiles were associated with increased hypertension prevalence, and hypertensive individuals exhibited significantly higher LDH levels compared to normotensives.[53,54] In a spontaneous hypertension animal model, high lactate concentrations induced and exacerbated renal fibrosis through TRPV4-TGFβ1-SMAD2/3-CTGF-mediated pathways.[55] These findings highlight the importance of considering, beyond the established factors of diabetes duration, creatinine, blood lipids, and blood pressure, the potential impact of elevated LDH and lactate associated with glucose metabolism disturbances in DM patients on DKD progression. While further research is needed to elucidate the precise relationships and mechanisms involved in lactate and DKD, these initial observations warrant further investigation.

Our study provided a novel perspective on DKD prediction by demonstrating that risk factors vary based on serum lactate levels in T2DM patients. While traditional prediction factors of nomograms like those reported in previous studies remained relevant,[17,18] we identified distinct predictors for DKD in patients with normal and high lactate levels. By incorporating these lactate-related factors into easy-to-use nomograms, we empowered clinicians to make personalized and early DKD predictions, facilitating timely intervention and potentially delaying the progression to end-stage renal disease. Despite the significance of our findings, the study has limitations. Being a retrospective cross-sectional study, causal relationships among lactate levels, risk factors, and DKD require further exploration through cohort and mechanism studies. Additionally, our analysis was based on available cohort data and may not encompass all DKD risk factors, necessitating inclusion of more biomarkers in future studies. Moreover, as a single-center study, our findings may not be universally applicable, urging inclusion of patients from multiple centers to enhance model accuracy and practicality.

Conclusions

In conclusion, the serum lactate level-based nomogram models, combined with conventional risk factors, offer an effective tool for predicting DKD probability in T2DM patients. This approach holds promise for early risk assessment and tailored intervention strategies.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author (Yong Xu) on reasonable request.

Ethics Approval and Consent to Participate

All protocols followed the ethical guidelines of the Declaration of Helsinki, and the study has been approved by the Ethics Committee of the Affiliated Hospital of Southwest Medical University (license number: KY2023142). When we retrospectively collected the data of previous cases, written informed consent was waived due to the retrospective nature and low risk of the study. We obtained informed consent when collecting blood and urine from healthy people.

Acknowledgments

Author Contributions

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

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Disclosure

The authors declare that they have no competing interests.

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