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ORIGINAL RESEARCH

Two-Dimensional Ultrasound-Based Radiomics Nomogram for Diabetic Kidney Disease: A Pilot Study

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Objective: To establish a radiomics nomogram based on two-dimensional ultrasound for risk assessment of diabetic kidney disease (DKD) in patients with type 2 diabetes mellitus (T2DM).

Methods: This study retrospectively collected two-dimensional ultrasound images and clinical data from 52 patients with T2DM who underwent renal biopsy in our hospital from January 2023 to August 2023. Based on the pathological results, all patients were categorized into two groups: DKD (n=33) and non-DKD (n=19). The radiomic features of the segmented kidney in ultrasound pictures were retrieved and selected to calculate each patient's rad-score. A predictive nomogram based on rad-score and clinical features was then constructed and validated based on the calibration curve.

Results: The rad-score for all patients were computed based on five imaging characteristics extracted from the ultrasound images. The predictive nomogram was developed with the rad-score, diabetic retinopathy, duration of diabetes, and glycosylated hemoglobin. Moreover, This radiomics nomogram showed outstanding calibration capability, discrimination as well as therapeutic usefulness.

Conclusion: We constructed a nomogram based on two-dimensional ultrasound for DKD in T2DM patientsThe model has been proven to have good predictive performance, showing its potential in identifying DKD in T2DM patients and assisting in making appropriate early interventions.

Keywords: diabetic kidney disease, rad-score, two-dimensional ultrasound, machine learning, nomogram

Introduction

Diabetic kidney disease (DKD) is the most prevalent and severe microvascular complication in patients with type 2 diabetes mellitus (T2DM). It is a leading cause of end-stage renal disease (ESRD) in China and developed countries.[1] Prior research has indicated that early diagnosis and treatment could significantly delay the progression of ESRD and improve patients' prognosis.[2]

Currently, the gold standard for DKD is renal biopsy. However, this procedure is invasive and carries potential bleeding risks. Given that diabetic patients inherently have a higher risk of bleeding and there is no superior treatment method available post-diagnosis of DKD, the decision to perform a kidney biopsy and the timing of such a procedure are critical. In light of the absence of a consensus and guidelines, there is an urgent need for more evidence to support and clarify the clinical threshold for nephrologists to perform renal biopsies in patients with diabetes.

Two-dimensional ultrasound is currently the preferred and routine imaging method for patients with kidney disease. However, it lacks specificity in detecting DKD, prompting the development of more accurate identification techniques. Recently, radiomics methods have shown promise in identifying a variety of illnesses, including kidney disease, by extracting high-throughput picture feature information and performing data conversion and analysis. The majority of existing research on DKD prediction is concerned with assessing and predicting clinical data from DKD patients.[3–5]

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Moreover, a recent study demonstrated that the parameters of diffusion-weighted magnetic resonance imaging could serve as a biomarker to identify T2DM patients with the diagnosis of DKD and higher ESRD risk categories.[6] However, these studies lack a combined risk prediction model that incorporates clinical data and two-dimensional ultrasound pictures. The purpose of this study is to investigate the predictive value of a machine-learning model based on ultrasound radiomics for detecting DKD in T2DM patients.

Methods

Study Population

A retrospective study was conducted on 613 patients who underwent renal biopsy at Renmin Hospital of Wuhan University from January 1, 2023, to August 31, 2023. The inclusion criteria were: 1) initial kidney biopsy with conclusive pathological findings; 2) T2DM. The exclusion criteria were: 1) previous renal biopsy (n=29); 2) Clinically diagnosed as DKD and the subsequent treatment had begun (n=398); 3) other types of diabetes (n=56); 4) lack of clinical data or unclear ultrasound images (n=78). Finally, a total of 52 patient data were included in the study This study was approved by the Ethics Committee of Renmin Hospital of Wuhan University (No.: WDRY2019-G001 (X03)) and informed consent was waived.

Imaging Collection and Analysis

All patients had bilateral renal ultrasounds performed utilizing a GE Vivid iq ultrasound diagnostic device and a C5-1 probe. These exams were done by the same doctor, who has over five years of expertise in ultrasound diagnostics. For each patient, two two-dimensional ultrasound pictures of the biggest portion with a distinct contour were saved. The Region of Interest (ROI) was then identified along the renal cortex using Darwin software. This work was completed by a doctor with over 5 years of expertise in renal ultrasonography diagnosis, which was confirmed by another doctor with 10 years of experience in the same field. After that, 1125 radiomics eigenvalues were recovered utilizing Darwin's platform (https://arxiv.org/abs/2009.00908). These eigenvalues comprised six types of images (original, exponential, gradient, logarithm, square, square-root) and six types of features (first-order, GLCM, GLDM, GLRLM, GLSZM, and NGTDM). To screen the radiomics characteristics, we used two machine learning methods: least absolute shrinkage and selection operator regression (LASSO) and support vector machine recursive feature elimination (SVM-RFE). To avoid overfitting, we calculated the intersection of the features chosen by these two approaches. As a consequence, five radiomics traits were identified. We then computed radiomics scores for each subject. Figure 1 illustrates the research method.

Clinical Data Collection

The clinical data of all patients in this hospital, including age, sex, course of type 2 diabetes, history of retinopathy, history of hypertension, and so on. Moreover, laboratory indexes examined within one week before renal biopsy were also collected.

Statistical Analysis

All the data were statistically analyzed by using IBM SPSS 20.0 and R 3.3.3 software. When the measured data conformed to the normal distribution, the *t*-test was used for pairwise comparison, the *U*-test was used for non-normal distribution, and the χ^2 test was used for comparison of the counted data. Univariate and multivariate logistic regression were used to analyze the independent risk factors of DKD in T2DM patients and to construct a nomogram model. The calibration curve is used to verify the prediction model internally, and the receiver operating characteristic curve (ROC) and decision curve are used to evaluate the prediction efficiency of the model. $P<0.05$ was statistically significant.

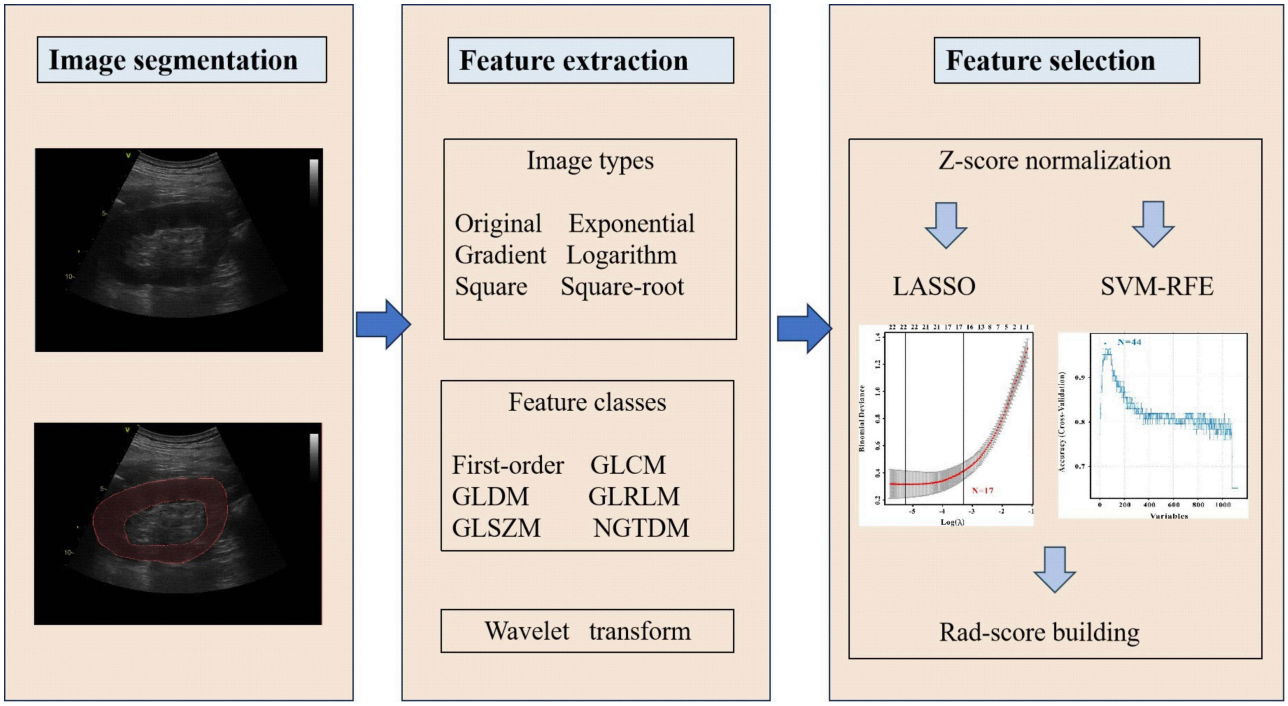

Figure 1 The workflow of the critical steps in constructing an ultrasound imaging-based rad-score for a patient with Type 2 diabetes.

Results

Participant Characteristics

This study comprised 52 patients: 41 men (78.8%) and 11 females (21.2%), with an average age of 55.4±11.4 years and a range of 30–77 years. Pathological testing revealed that 33 cases (63.5%) of the 52 patients had DKD and 19 cases (36.5%) did not. Pathology revealed four cases of hypertensive renal damage, three cases of IgA, two cases of glomerular minor lesions, two cases of membranous nephropathy, two cases of acute interstitial nephritis, two cases of focal segmental glomerulosclerosis, one case of nodular glomerulopathy, one case of minimal pathological nephropathy, and lupus nephritis. Patients with DKD have higher levels of glycosylated hemoglobin, low-density lipoprotein cholesterol, and lower thrombin time compared to non-DKD patients. They also have a higher proportion of diabetic retinopathy and a longer course of diabetes (all P<0.05). However, there are no statistical differences in age, sex, history of hypertension, kidney length, cortical thickness, liver function, renal function, blood routine, and electrolytes between the two groups (Table 1).

Table 1 The Baseline Characteristics of All Patients

Characteristics	No DKD (n=19)	DKD (n=33)	P value
Age, years old	57.1 ± 11.0	54.5 ± 11.6	0.433
Gender, male, n (%)	14 (73.7)	27 (81.8)	0.735
Comorbidity, n (%)			
Hypertension	12 (63.2)	19 (57.6)	0.919
Diabetic retinopathy	8 (42.1)	27 (81.8)	0.008
Duration of diabetes, n (%)			0.023
≥ 10 years	2 (10.5)	15 (45.5)	
<10 years	17 (89.5)	18 (54.5)	
Ultrasound parameters			
Kidney length, cm	10.2±0.9	10.5±0.8	0.265
Cortical thickness, cm	1.2±0.3	1.2±0.2	0.236

(*Continued*)

Table 1 (Continued).

Characteristics	No DKD (n=19)	DKD (n=33)	P value
Laboratory results			
White blood cells, $\times 10^9$/L	14.8 ± 6.3	11.4 ± 5.5	0.392
Hemoglobin, mg/L	124.3 ± 29.8	113.2 ± 20.1	0.116
Platelet, $\times 10^9$/L	243.1 ± 78.7	232.9 ± 71.2	0.687
Serum albumin, g/L	36.2 ± 9.2	37.8 ± 8.0	0.526
Blood urea nitrogen, mmol/L	9.3 ± 3.8	11.3 ± 4.3	0.187
Creatinine, μmol/L	149.6 ± 62.3	163.5 ± 76.9	0.696
eGFR, mL/min	68.4 ± 28.5	56.5 ± 27.2	0.196
Glucose, mmol/L	9.5 ± 3.3	9.3 ± 3.7	0.873
HbA1c, %	6.5 ± 0.8	7.7 ± 2.0	0.015
Total cholesterol, mmol/L	5.8 ± 2.3	4.8 ± 1.5	0.151
Triglyceride, mmol/L	2.8 ± 1.3	2.2 ± 1.1	0.262
HDL-C, mmol/L	1.1 ± 0.3	1.2 ± 0.5	0.550
LDL-C, mmol/L	1.8 ± 0.5	2.7 ± 0.9	<0.001
Prothrombin time, s	11.3 ± 1.2	11.1 ± 1.2	0.541
APTT, s	28.2 ± 4.2	26.6 ± 2.7	0.101
D-dimer, mg/L	1.1 ± 0.5	0.8 ± 0.4	0.422
Hs-CRP, mg/L	1.9 ± 0.9	2.6 ± 1.3	0.365
Potassium, mmol/L	3.7 ± 1.1	4.2 ± 0.8	0.087
Sodium, mmol/L	139.4 ± 3.1	139.4 ± 2.9	0.926
Calcium, mmol/L	2.1 ± 0.2	2.1 ± 0.2	0.796
Proteinuria, n (%)			0.212
-	6 (31.6)	5 (15.2)	
≤ 1+	8 (42.1)	16 (48.5)	
≥ 2+	5 (26.3)	12 (36.3)	
Hematuria, n (%)			0.222
-	12 (63.2)	15 (45.5)	
≤ 1+	4 (21.1)	9 (27.3)	
≥ 2+	3 (15.7)	9 (27.2)	

Abbreviations: DKD, diabetic kidney disease; eGFR, estimate glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein.

Calculation of Imaging Score

We extracted 1125 image features from each two-dimensional ultrasound picture of the kidney, with 17 and 44 image features evaluated using LASSO regression and SVM-RFE, respectively (Figure 2A and B). Finally, the two machine learning approaches shared five characteristics, which were utilized to compute the picture score (Figure 2C and D). The Rad-score in the DKD group was considerably greater than the non-DKD group (0.62 0.30 vs 0.31 0.20, P<0.001). ROC data indicate that the rad-score has high diagnostic effectiveness (AUC=0.795, 95% CI 0.676–0.921, P<0.001, Figure 3B).

The Construction of Nomogram of Imaging Science

We analyzed all patients' clinical data and rad-scores using univariate and multivariate logistic regression (Table 2). Diabetic retinopathy (OR = 5.98, 95% CI 1.19–34.94, P = 0.037), diabetes duration (OR = 1.76, 95% CI 1.14–2.72, P = 0.011), glycosylated hemoglobin (OR = 4.02, 95% CI 1.40–11.59, P = 0.010), and rad-score (OR = 7.97, 95% CI 1.25–50.78, P = 0.028) were identified as independent risk factors for DKD in T2DM patients. Based on these findings, we developed a nomogram model to predict DKD risk in T2DM patients (Figure 3A). In this paradigm, each index corresponds to a place on the corresponding axis in the diagram. The number on the scoring scale indicates the index's score. The point on the risk value axis corresponding to this total score represents the probability of the patient having DKD.

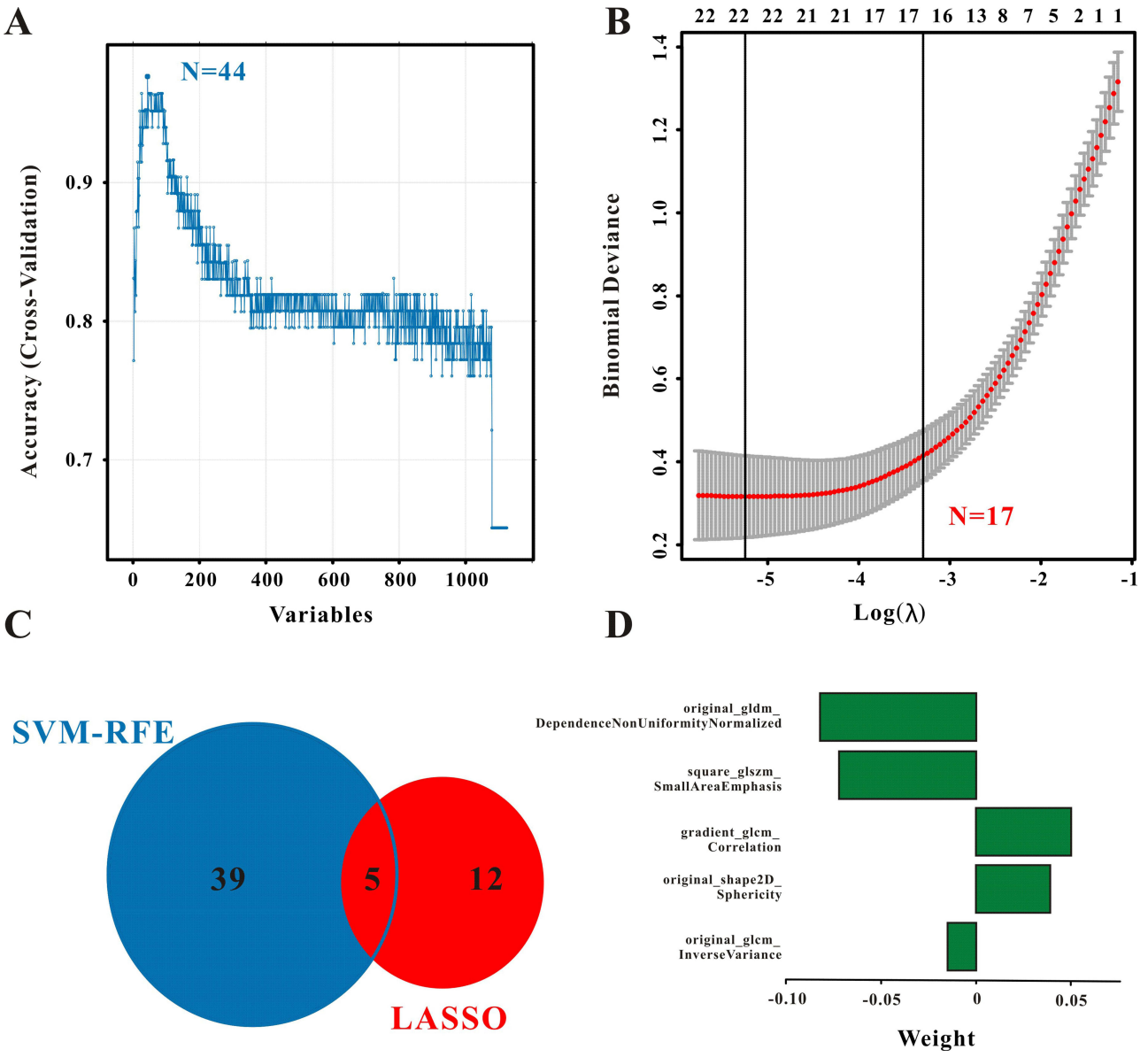

Figure 2 Radiomics feature selection using LASSO and SVM-RFE regression for establishing the rad-score. (**A**) LASSO coefficient distribution of all the radiomics features. (**B**) SVM-RFE regression for all the features. (**C**) The overlapping of features of the SVM-RFE and LASSO regression. (**D**) The weights of the selected radiomics features.

Evaluation of Radiomics Nomogram

The array graph model showed significant discriminatory capacity, with an Area Under the Curve (AUC) of 0.878 and a 95% Confidence Interval (CI) spanning from 0.782 to 0.974 ($P < 0.001$, Figure 3B). The calibration curve showed an excellent match for the model ($\chi^2 = 11.2$, $P = 0.183$, Hosmer-Lemeshow test, see Figure 3C). Furthermore, the clinical decision curve demonstrated that the model is very clinically applicable (Figure 3D).

Example of Radiomics Nomogram

For example, a 58-year-old patient with diabetes for 15 years had retinopathy, an HbA1c of 5.2 mmol/L, and a rad-score of one. The comparable scores were 2.25 points for a history of diabetes, 3.75 points for retinopathy, 1 point for HbA1c, and 7 points for rad-score. The overall score was 14 points, and the risk of DKD is about 90%.

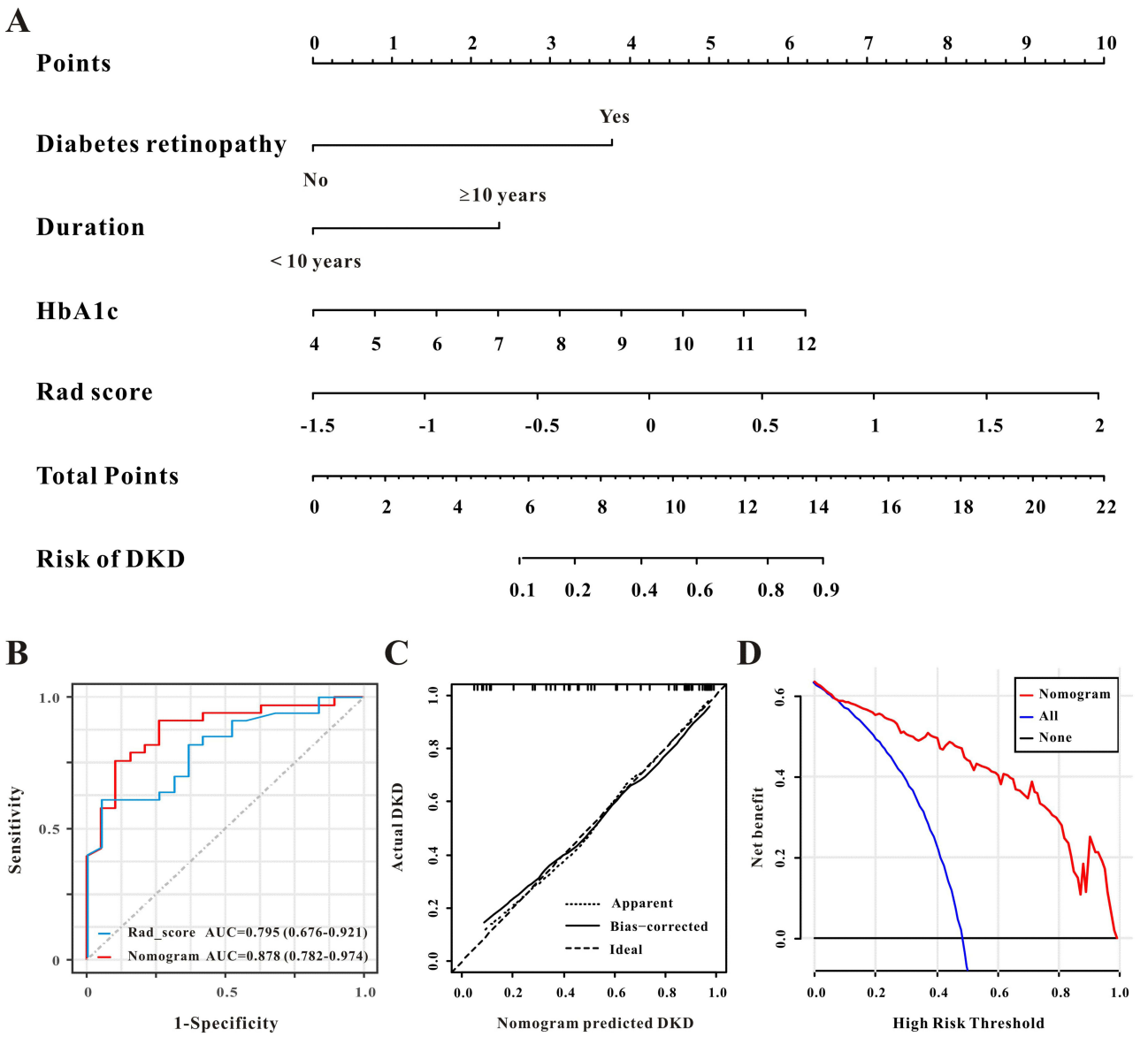

Figure 3 (**A**) The radiomics nomogram for the risk of DKD in diabetic patients. The receiver operating characteristic curve (**B**), the calibration curve (**C**), and the decision curve analysis (**D**) of the radiomics nomogram for DKD.

Discussion

In recent years, advances in big data research have resulted in the widespread use of machine learning algorithms in radiomic-based risk prediction models. In the field of tumor diagnostics, Ya Sun et al[7] used machine learning approaches to conduct a thorough examination of transrectal ultrasonography and contrast-enhanced ultrasound (CEUS). This method significantly increased the detection rate of peripheral zone prostate cancer. In terms of tumor therapy, Feu-Hong Yu et al[8] investigated the predicted efficacy of a Deep Learning Radiomics model that combines pre-treatment ultrasound imaging data with clinical features. This model was used to assess the treatment response of breast cancer patients after neoadjuvant chemotherapy. Furthermore, Fei Meng et al[9] developed an SVM-based prediction model for fibrosis in patients with alcoholic fatty liver disease. This model integrates clinical data and multimodal radiomics characteristics to identify individuals at risk of fibrosis development, improving the management of nonalcoholic fatty liver disease and T2DM. This research offers fresh ideas and approaches for using machine learning to better anticipate and diagnose various illnesses.

Table 2 Univariate and Multivariate Logistic Regression Analysis for DKD

	Univariate		Multivariate	
	OR (95% CI)	**P**	**OR (95% CI)**	**P**
Age	0.98 (0.93–1.03)	0.426		
Gender, male	1.61 (0.42–8.21)	0.491		
Hypertension	0.79 (0.25–2.53)	0.693		
Diabetic retinopathy	4.19 (1.74–16.02)	0.005	5.98 (1.19–34.94)	0.037
Duration of diabetes	1.77 (1.24–2.54)	0.002	1.76 (1.14–2.72)	0.011
Kidney length	1.48 (0.72–2.96)	0.262		
Cortical thickness	4.90 (0.36–66.52)	0.232		
White blood cells	0.98 (0.94–1.02)	0.401		
Hemoglobin	0.98 (0.96–1.01)	0.121		
Platelets	1.00 (0.99–1.01)	0.681		
Serum albumin	1.02 (0.96–1.10)	0.518		
Blood urea nitrogen	1.09 (0.96–1.24)	0.191		
Creatinine	1.00 (0.99–1.01)	0.690		
eGFR	0.99 (0.97–1.01)	0.197		
Glucose	0.99 (0.90–1.10)	0.870		
HbA1c	1.78 (1.08–2.95)	0.025	4.02 (1.40–11.59)	0.010
Total cholesterol	0.83 (0.62–1.10)	0.186		
Triglyceride	0.85 (0.63–1.15)	0.281		
High-density lipoprotein cholesterol	1.44 (0.41–4.73)	0.544		
Low-density lipoprotein cholesterol	2.12 (1.92–8.45)	0.023	4.18 (0.84–24.16)	0.136
Prothrombin time	0.85 (0.51–1.42)	0.534		
Activated partial thromboplastin time	0.86 (0.71–1.04)	0.121		
D-dimer	0.83 (0.53–1.31)	0.425		
High-sensitivity C-reactive protein	1.12 (0.88–1.42)	0.367		
Potassium	1.74 (0.89–3.40)	0.106		
Sodium	0.99 (0.82–1.20)	0.924		
Calcium	0.62 (0.20–20.92)	0.791		
Proteinuria				
-	Ref.	-		
≤ 1+	2.40 (0.56–10.32)	0.240		
≥ 2+	2.88 (0.59–13.99)	0.190		
Hematuria				
-	Ref.	-		
≤ 1+	1.80 (0.44–7.31)	0.411		
≥ 2+	2.40 (0.53–10.88)	0.256		
Rad-score	5.14 (1.96–13.47)	0.001	7.97 (1.25–50.78)	0.028

Abbreviations: DKD, diabetic kidney disease; eGFR, estimate glomerular filtration rate.

Prior risk prediction models for diabetic kidney disease were mostly based on the examination of enormous amounts of clinical and laboratory data. However, no research has used a nomogram of radiomics scores in combination with ultrasound pictures. Sun L et al[3] studied 14,628 individuals with T2DM and identified four independent predictors: age, urine albumin-to-creatinine ratio, estimated glomerular filtration rate, and neutrophil percentage. These predictors were used to create a nomogram, which yielded a C-index of 0.864. Wang et al[4] conducted another investigation on clinical data from 2163 diabetes patients who were hospitalized. A unique logistic regression model was used to identify relevant variables, resulting in the development of a simpler model for detecting DKD instances among diabetic patients. Furthermore, Zou Y et al[10] analyzed the clinical data of 390 DKD patients and created a research model to predict the probability of end-stage renal disease. Tan HZ et al[11] examined 102 individuals with T2DM. They observed that the length of T2DM, HbA1c levels, absence of hematuria, presence of diabetic retinopathy, and lack of positive systemic

biomarkers were all independent predictors of DKD. The univariate analysis revealed that DKD patients were more likely to have hypertension, a longer duration of T2DM, a higher prevalence of diabetic retinopathy, and relatively higher baseline HbA1c levels. However, hypertension was excluded in the multivariate model. These findings are consistent with our results.

This research looked at the age and gender of all individuals with T2DM. Regardless of whether they have DKD, male patients outnumber females. DKD patients were typically younger and had diabetes for a longer period time, suggesting that diabetes beginning sooner increases the risk of developing diabetic kidney disease. Patients with DKD were more likely than those without to have a history of diabetic retinopathy or hypertension. The duration of diabetes, the existence of diabetic retinopathy, and glycosylated hemoglobin levels were identified as independent risk factors for the development of DKD in diabetic individuals by multivariate regression analysis. The radiomics score (rad score) for each patient was determined by extracting five characteristics from ultrasound pictures. The radiomics nomogram, which included diabetic retinopathy, diabetes duration, HbA1c, and rad scores, outperformed the clinical nomogram, which excluded the rad score.

Renal ultrasonography is becoming a regular practice in physical exams. The use of artificial intelligence greatly decreases the time necessary to evaluate 2D ultrasound pictures, resulting in considerable savings. It is practically feasible to deliver picture information that standard 2D ultrasonography cannot provide for clinical risk assessment. This research is a retrospective analysis. To reduce the influence of machine variations on image analysis results, photos from the same machine were intentionally chosen, resulting in a limited sample size. Despite this, the study is exploratory, relying on normal clinical procedures and readily available information, and has produced encouraging preliminary results. Future research will necessitate multi-center investigations with bigger sample numbers to confirm the conclusions of this study.

Conclusions

The radiomics nomogram we developed, based on two-dimensional ultrasonography, can first predict the likelihood of DKD in diabetic individuals and has shown high predictive efficacy. Larger sample sizes may be required in future research to further validate this model. This is a positive step toward better early identification and management of DKD.

Data Sharing Statement

The datasets used in this study are available from the corresponding author.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Renmin Hospital of Wuhan University (No.: WDRY2019-G001 (X03)).

Informed Consent Statement

Patient consent was waived due to the reason that this was a retrospective observational study and did not add any costs to patients or do any harm to them.

Author Contributions

All authors made substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit it to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there is no conflict of interest in this work.

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