Original Article

Clinical Prediction Score for Diagnosing Non-Diabetic Kidney Disease in Patients with Type 2 Diabetes Mellitus

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Background: When non-diabetic kidney disease (NDKD) is suspected, biopsy proven is used for definite diagnosis. However, there are not always easily available and may lead to cause complications. A clinical prediction score may help selecting appropriate patients for kidney biopsy.

Objective: To develop a clinical prediction score for distinguishing any type of NDKD (NDKD alone or coexisting NDKD and diabetic nephropathy [DN]) and DN alone.

Materials and Methods: A retrospective cohort study was conducted in type 2 diabetes mellitus (T2DM) patients with atypical features of DN, who had kidney biopsy at Thammasat University Hospital between 2011 and 2019. The present study divided patients into NDKD alone, coexisting NDKD and DN, and DN alone, confirmed by pathological diagnoses. The authors developed a clinical prediction score by weighing coefficients of predictors in a multivariable logistic model. Internal validation was performed with bootstrapping.

Results: The present study included 81 patients of which 28 (34%) had NDKD alone, 15 (18%) had coexisting NDKD and DN, and 38 (41%) had DN alone. Primary membranous nephropathy, primary focal segmental glomerulosclerosis (FSGS), and secondary FSGS were prevalent in any NDKD. Absence of diabetic retinopathy (DR) showed a significant association with any NDKD (adjusted OR 3.72; 95% CI 1.28 to 10.8; p=0.02). The prediction score, AUROC of 0.75 (95% CI 0.63 to 0.86), had four predictors, duration of DM of less than 10 years, eGFR of more than 30 mL/minute/1.73 m^2, HbA1c of less than 8%, and absence of DR. Higher scores were associated with higher probability of NDKD.

Conclusion: The present study clinical prediction score appears to be a useful tool to determine NDKD probability. T2DM patients with atypical presentation of DN with lower scores (0 to 2) may defer kidney biopsy.

Keywords: Non-diabetic kidney disease; clinical prediction score; kidney biopsy; type 2 diabetes mellitus

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Diagnosing non-diabetic kidney disease (NDKD) in patients with type 2 diabetes mellitus (T2DM) is often problematic and typically requires a kidney biopsy for definite diagnosis. The common pathological diagnoses of NDKD are membranous nephropathy (MN), focal segmental glomerulosclerosis (FSGS), and IgA nephropathy[1-3]. Unfortunately, it remains difficult to diagnose as NDKD may present alone or in combination with diabetic nephropathy (DN), the latter obscures the classical presentation of each disease. Thus, kidney biopsy is the standard investigation for definite diagnosis non-diabetic glomerular disease[4]. However, this invasive procedure may have bleeding complications and its availability is limited in some resource-constrained hospitals.

The decision to perform kidney biopsy depends on the likelihood of NDKD. According to the Kidney Disease Outcomes Quality Initiative (KDOQI) guideline[4], patients with atypical presentations of DN with the absence of diabetic retinopathy (DR), low or rapidly declining glomerular filtration rate (GFR), rapidly increasing proteinuria or nephrotic syndrome, the presence of active urinary sediment, or signs and symptoms of systemic disease, should be evaluated for NDKD. Even using these criteria,

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NDKD prevalence was found in only half of some biopsy reports[1,5-7]. It appears there is a knowledge gap toward improving NDKD diagnostic performance.

Previous studies have only reported predictors, such as absence of DR, duration of diabetic mellitus (DM), degrees of proteinuria, hemoglobin A1c (HbA1c), or levels of creatinine or GFR associated with NDKD, but none have mentioned the utility of a combined predictive probability[3,7-9]. A clinical prediction score, so-called clinical decision rules, combines predictors in the model, informs clinicians and patients about disease probability, and can aid in decision-making[10]. In the present study, the authors aimed to develop a simplified clinical prediction score for NDKD to help determine the appropriate clinical setting for kidney biopsy in T2DM with atypical presentation.

Materials and Methods

Data were collected by retrospective medical chart review included all patients with T2DM that undergone kidney biopsy with age were greater than or equal to 18 years old at Thammasat University Hospital between January 2011 and December 2019. The diagnosis of T2DM was obtained from history and criteria established by the American Diabetes Association[11]. Excluded criteria were patients with history of kidney transplantation and inadequate specimen for interpreting pathological diagnosis from kidney biopsy. The present study was approved by the Human Research Ethics Committee of Thammasat University No 1 (Faculty of Medicine), certificate of approval 130/2020.

The authors collected all clinical parameters including age, gender, body mass index (BMI), duration of DM, presence of DR, hypertension, established cardiovascular diseases (CVD), and indications for kidney biopsy. The presence of DR was examined and recorded by an ophthalmologist. The duration of DM referred to the time from first diagnosis to kidney biopsy. Hypertension was defined as either having a recorded history of hypertension or systolic blood pressure greater than or equal to 140 mmHg or diastolic blood pressure greater than or equal to 90 mmHg, determined at clinical evaluation for kidney biopsy in the absence of any antihypertensive drug. CVD was a history of myocardial infarction or congestive heart failure in previous medical records.

Laboratory results were collected at the time of biopsy and included complete blood count (CBC), blood urea nitrogen (BUN), serum creatinine using enzymatic method with estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)[12], urinary analysis, urine protein creatinine ratio (UPCR), fasting plasma glucose (FPG), and HbA1c. Hematuria was defined as a red blood cell (RBC) count of greater than or equal to 3 cells in urine examination. UPCR was calculated by dividing urine protein (mg/dL) by urine creatinine (mg/dL).

All kidney specimens were examined using light microscope and immunofluorescence assay. Because the authors' hospital did not routinely perform electron microscope, very few cases had these results. DN diagnosis and classification were made using criteria established by the Renal Pathology Society in 2010[13]. Although, there was a difficulty to differentiate between FSGS and advanced stage of DN by light microscope alone, pathologists used other circumstantial features, such as nodular sclerosis or hyalinosis, to be clues for diagnosis of DN. The pathological diagnosis was divided into three groups consisting of DN, NDKD, and coexisting DN and NDKD (DN+NDKD).

Statistical analysis

All statistical analyses were performed using Stata Statistical Software, version 16.0 (StataCorp LLC, College Station, TX, USA). All p-values were two-sided; p-value of less than 0.05 was considered statistically significant. The complete-case analysis was used for all analyses. Continuous variables data were presented as mean ± standard deviation (SD) or median and interquartile range (IQR). Categorical variables were expressed as frequency and percentages.

Model development

In the processes of model specification, the authors reviewed literature, which reported predictors of NDKD, and explored associations with any type of NDKD, which were NDKD alone or DN+NDKD, in a univariable logistic model. Any predictors, in which p was smaller than 0.2 in univariable analyses, were selected for multivariable logistic regression[14]. Then, the authors tested the performance of the final model with Hosmer-Lemeshow test for calibration or goodness-of-fit, and area under receiver operating characteristic curve (AUROC) for discrimination.

To generate the clinical prediction score, coefficients of all predictors were weighed by dividing the lowest coefficient and rounded into integers. The

Table 1. Baseline characteristics

Characteristics[a]	Total (n=81); n (%)	DN (n=38); n (%)	NDKD (n=28); n (%)	DN+NDKD (n=15); n (%)
Age (year); mean±SD	56.0±13.1	54.1±12.7	58.4±14.2	56.3±12.2
Male	41 (50.6)	19 (50.0)	13 (46.4)	9 (60.0)
BMI (kg/ m^2); mean±SD	25.6±5.5	25.2±4.6	25.5±6.5	26.8±5.5
Duration of DM (years); median [IQR]	8 [4, 12]	10 [6, 12]	5 [3, 10]	5 [3, 10]
Duration >10 years	37 (45.7)	22 (57.9)	10 (35.7)	5 (33.3)
Presence of DR	39 (48.2)	24 (63.2)	7 (25.0)	8 (53.3)
Hypertension	71 (87.7)	34 (89.5)	23 (82.1)	14 (93.3)
Established CVD	11 (13.6)	6 (15.8)	2 (7.1)	3 (20.0)
Serum creatinine (mg/dL); mean±SD	2.7±1.6	2.9±1.7	2.5±1.7	2.3±1.3
eGFR (mL/minute/1.73 m^2); mean±SD	37.0±29.0	31.6±24.9	42.3±34.5	40.6±26.8
eGFR category				
>60	17 (21.0)	5 (13.2)	8 (28.6)	4 (26.7)
30 to 60	20 (24.7)	9 (23.7)	6 (21.4)	5 (33.3)
<30	44 (54.3)	24 (63.2)	14 (50.0)	6 (40.0)
Hb (g/dL); mean±SD	10.7±2.3	10.5±1.8	11.0±2.9	10.8±2.4
Hematuria	59 (72.8)	30 (79.0)	18 (64.3)	11 (73.3)
Urine RBC (cell/HPF)				
0 to 3	22 (27.2)	8 (21.1)	10 (35.7)	4 (26.7)
3 to 30	42 (51.9)	24 (63.2)	9 (32.1)	9 (60.0)
>30	17 (21.0)	6 (15.8)	9 (32.1)	2 (13.3)
UPCR (mg/g); mean±SD	8.3±6.7	9.2±7.0	7.0±7.0	8.7±5.0
UPCR category (mg/g)				
<0.5	2 (2.5)	0 (0.0)	2 (7.1)	0 (0.0)
0.5 to 3.0	15 (18.5)	6 (15.8)	9 (32.1)	0 (0.0)
>3.0	64 (79.0)	32 (84.2)	17 (60.7)	15 (100)
FPG (mg/dL); mean±SD	149±85	156±81	144±107	141±55
HbA1c (%); mean±SD	7.5±1.8	7.8±1.9	6.9±1.5	7.4±1.7

DN=diabetic nephropathy; NDKD=non-diabetic kidney disease; BMI=body mass index; DM=diabetes mellitus; DR=diabetic retinopathy; CVD=cardiovascular disease; eGFR=estimated glomerular filtration rate; Hb=hemoglobin; RBC=red blood cell; UPCR=urine protein creatinine ratio; FPG=fasting plasma glucose; HbA1c=hemoglobin A1c; SD=standard deviation; IQR=interquartile range

[a] Data are presented as mean ± SD for continuous variables, number (percent) for categorical variables (percentages may not total 100 due to rounding), or median [IQR] for non-normal distributed variables

scores of individual patients were matched with the estimated probability of it being NDKD in the final model, also referred to as the developed model. Next, these individual scores were tested for discrimination performance using AUROC.

The authors performed internal validation using a bootstrapping procedure with a 1,000-bootstrap sample. This procedure quantified the optimism of the developed model[15]. The authors revised the new model, now called the optimism-adjusted model using the uniform shrinkage factor. Then, the scores of individual patients were matched again with estimated probability in this optimism-adjusted model. AUROC was again tested.

Sample size

Sample size calculation was based on number of events per variable (EPV) for logistic analysis in a simulation study[16], which was at least 10 EPV. Based on review literature[1], the prevalence of NDKD in T2DM was 45% to 75%. The authors assumed 50% of NDKD in the cohort. Thus, the estimated study size was at least 80 to achieve four predictors in the final model.

Results

Eighty-one T2DM patients, who had kidney biopsies, were included. Indications of kidney biopsy were the sudden onset of proteinuria or nephrotic

Table 2. Pathological diagnosis of NDKD

Pathological diagnosis[a]	Total NDKD (n=43); n (%)	NDKD (n=28); n (%)	DN+NDKD (n=15); n (%)
Primary FSGS	6 (14.0)	6 (21.4)	0 (0.0)
Primary membranous nephropathy	6 (14.0)	4 (14.3)	2 (13.3)
Pauci-immune glomerulonephritis	5 (11.6)	4 (14.3)	1 (6.7)
Lupus nephritis	2 (4.6)	2 (7.1)	0 (0.0)
IgA nephropathy	5 (11.6)	3 (10.7)	2 (13.3)
Post-infectious glomerulonephritis	5 (11.6)	1 (3.6)	4 (26.7)
Secondary FSGS	6 (14.0)	3 (10.7)	3 (20.0)
Hypertensive nephrosclerosis	3 (7.0)	3 (10.7)	0 (0.0)
Acute tubular necrosis	4 (9.3)	2 (7.1)	2 (13.3)
Acute interstitial nephritis	2 (4.7)	2 (7.1)	0 (0.0)
Thrombotic microangiopathy	1 (2.3)	1 (3.6)	0 (0.0)
Others	1 (2.3)	0 (0.0)	1 (6.7)

DKD=non-diabetic kidney disease; DN=diabetic nephropathy; FSGS=focal segmental glomerulosclerosis; IgA=immunoglobulin A

[a] All data are categorical variables and presented as number (percent). Percentages may not total 100 due to rounding.

syndrome (39.5%), rapidly decreasing eGFR (37%), acute glomerular nephritis (AGN) or rapidly progressive glomerular nephritis (RPGN) (12.4%), and others (11%). Of the 81 patients, 38 (46.9%) were DN alone, 28 (34.6%) were NDKD alone, and 15 (18.5%) were DN+NDKD.

The baseline clinical characteristics of all patients, as well as DN, NDKD, and DN+NDKD groups, are shown in Table 1. Mean age of all patients was 56.0±13.1 years. The number of males and females were proportional. Median duration of DM was highest in the DN group being about 10 years, with an average of five years for both NDKD and DN+NDKD group. Presence of DR was predominantly high in the DN group, accounting for 63% of those cases, with 53% having DN+NDKD, and 25% NDKD. Mean eGFR was lowest in the DN group as 31.6 mL/minute/1.73 m², with 40.6 mL/minute/1.73 m² in DN+NDKD, and 42 mL/minute/1.73 m² in NDKD. Hematuria was found in high proportion in all three groups, but urine RBC of more than 30 cells/HPF predominated in the NDKD group. Mean HbA1c was 7.8% for the DN group, with 7.4% in the DN+NDKD group, and 6.9% in NDKD group.

Pathological findings of NDKD

Forty-three patients were diagnosed with some type of NDKD and included 28 NDKD alone and 15 DN+NDKD (Table 2). Primary membranous nephropathy, primary FSGS, and secondary FSGS were the three most common lesions, each accounting for 14%. Pauci-immune glomerulonephritis, IgA nephropathy, and postinfectious glomerulonephritis were also prevalent in these groups.

Predictors associated with NDKD

Univariable and multivariable binary logistic models were used to define associations for predictors and any type of NDKD including NDKD alone or DN+NDKD. As mentioned before, four predictors, which were duration of DM of less than 10 years, eGFR of more than 30 mL/minute/1.73 m², HbA1c of less than 8%, and absence of DR, were selected for the multivariable model due to their p-value being less than 0.2 in the univariable model. The absence of DR showed a significant association with NDKD with the highest magnitude of association (adjusted OR [aOR] 3.72; 95% CI 1.28 to 10.8; p=0.02), which meant a higher likelihood of NDKD. Other predictors, which demonstrated clinically significant magnitudes of association, but without statistical significance, were duration of DM of less than 10 years (aOR 1.50; 95% CI 0.52 to 4.35; p=0.46), eGFR of more than 30 mL/minute/1.73 m² (aOR 2.31; 95% CI 0.73 to 7.34; p=0.16), and HbA1c of less than 8% (aOR 2.82; 95% CI 0.79 to 10.0; p=0.11) (Table 3). The Hosmer-Lemeshow test was performed to test goodness-of-fit and demonstrated a p-value of 0.29. The AUROC of the model was 0.75 (95% CI 0.64 to 0.86) (Figure 1A).

Clinical prediction score

Within the present study multivariable model, the linear equation was: logodds (NDKD) = –1.75

Table 3. Univariable and multivariable binary logistic models to define the association of predictors in participants with any type of NDKD as compared to DN alone

Variables	Univariable model			Multivariable model[a,b]		
	OR	95% CI	p-value	aOR	95% CI	p-value
Age (per 1 year)	1.02	0.99 to 1.06	0.22			
Male	1.05	0.44 to 2.51	0.92			
BMI (per 1 kg/ m^2)	1.03	0.95 to 1.11	0.53			
Duration of DM <10 years	2.57	1.04 to 6.31	0.04	1.50	0.52 to 4.35	0.46
Absence of DR	4.48	1.70 to 11.8	<0.01	3.72	1.28 to 10.8	0.02
Hypertension	1.39	0.36 to 5.31	0.64			
Established CVD	1.43	0.40 to 5.11	0.59			
eGFR >30 mL/minute/1.73 m^2	1.97	0.81 to 4.80	0.14	2.31	0.73 to 7.34	0.16
Hemoglobin (per 1 g/dL)	1.08	0.89 to 1.31	0.46			
Absence of hematuria	1.81	0.66 to 4.96	0.25			
UPCR (per 1 mg/g)	0.96	0.90 to 1.03	0.27			
HbA1c <8%	2.47	0.88 to 6.88	0.09	2.82	0.79 to 10.0	0.11

OR=odds ratio; aOR=adjusted odds ratio; CI=confidence interval; BMI=body mass index; DM=diabetes mellitus; DR=diabetic retinopathy; CVD=cardiovascular disease; eGFR=estimated glomerular filtration rate; UPCR=urine protein creatinine ratio; HbA1c=hemoglobin A1c

[a] Predictors in multivariable model were selected using p-value <0.20 in univariable model.

[b] In the multivariable model (developed model), the equation is logodds (NDKD) = –1.75 + 0.41 (DM duration <10 years) + 0.84 (eGFR >30 mL/minute/1.73 m^2) + 1.03 (HbA1c <8%) + 1.31 (absence of DR). Odd ratios are calculated from exponentiation of coefficients in the model.

Table 4. The estimated probability being NDKD from developed model and optimism-adjusted model according to clinical prediction score

Score total[a]	Estimated probability being NDKD from	
	Developed model[b]	Optimism-adjusted model[c]
0	14.8%	21.1%
1	20.7%	26.7%
2	31.1%	35.8%
3	41.0%	43.8%
4	53.1%	53.2%
5	63.0%	61.0%
6	72.2%	68.4%
7	80.8%	76.0%
8	86.3%	81.2%

NDKD=non-diabetic kidney disease; DM=diabetes mellitus; eGFR=estimated glomerular filtration rate; HbA1c=hemoglobin A1c; DR=diabetic retinopathy.

[a] Score total is calculated from four predictors: score of 1 for "DM duration <10 years", score of 2 for "eGFR >30 mL/minute/1.73 m^2" and "HbA1c <8%", and score of 3 for "absence of DR"

[b] In developed model, the equation is logodds (NDKD) = –1.75 + 0.41 (DM duration <10 years) + 0.84 (eGFR >30 mL/minute/1.73 m^2) + 1.03 (HbA1c <8%) + 1.31 (absence of DR)

[c] In optimism-adjusted model, optimism was calculated from bootstrapping model with the uniform shrinkage factor of 0.77 and the revised intercept of –1.32. The equation is logodds (NDKD) = –1.32 + 0.31 (DM duration <10 years) + 0.65 (eGFR >30 mL/minute/1.73 m^2) + 0.80 (HbA1c <8%) + 1.02 (absence of DR)

+ 0.41 (DM duration of less than 10 years) + 0.84 (eGFR of more than 30 mL/minute/1.73 m^2) + 1.03 (HbA1c of less than 8%) + 1.31 (absence of DR). In here, the authors used the lowest coefficients of 0.41 as a denominator, and the weighted scores were assigned as 1 for DM duration of less than 10 years, 2 for eGFR of more than 30 mL/minute/1.73 m^2 and HbA1c of less than 8%, and 3 for absence of DR.

In Table 4, the authors compared the estimated probability of being NDKD from the developed and optimism-adjusted models. The score ranged from 0 to 8, with a higher score associated with greater probability of NDKD. The score was divided into three categories, low probability of NDKD with a score of 0 to 2, intermediate probability with a score of 3 to 5, and high probability with a score of 6 to 8 (Figure 2). The clinical prediction score had an AUROC of 0.75 (Figure 1B) and 0.70 in the optimism-adjusted model.

Discussion

The present study aimed to develop a tool for diagnosing NDKD in T2DM patients with atypical presentations of DN. The authors found some predictors that indicated when it was more likely for NDKD to occur, such as duration of DM, eGFR, HbA1c, and absence of DR. Clinical predictive scores

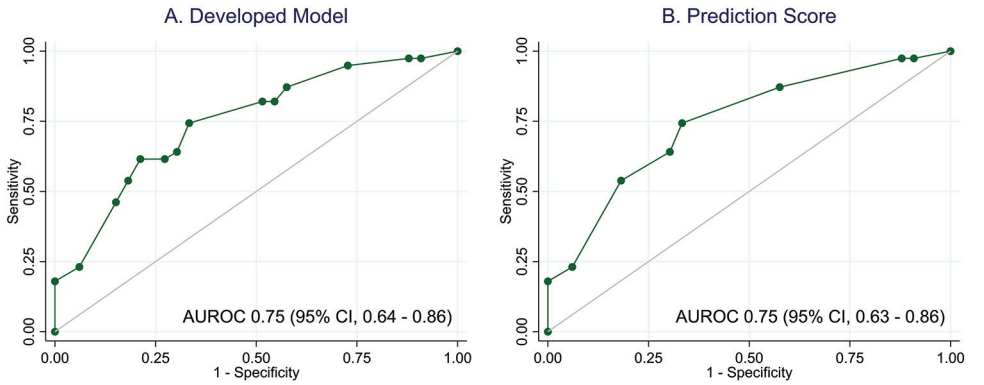

Figure 1. Receiver operating characteristic curve: (A) Developed model and (B) Prediction score.

AUROC=area under receiver operating characteristic curve; CI=confidence interval

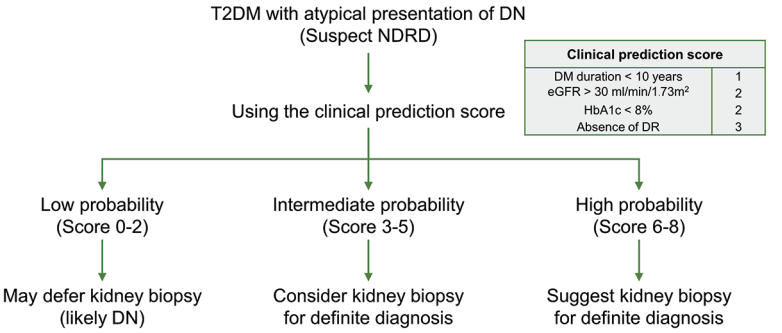

Figure 2. Proposed algorithm using the clinical prediction score.

A proposed algorithm for clinical use of the clinical prediction score, composed of four predictors and categorized into three groups. The low probability (score 0 to 2) of NDKD group means less likelihood of NDKD (or likely DN), which may defer kidney biopsy. The intermediate probability (score 3 to 5) and high probability for NDKD (6 to 8) suggests a kidney biopsy is necessary for definite diagnosis.

NDKD=non-diabetic kidney disease; DN=diabetic nephropathy; DM=diabetes mellitus; eGFR=estimated glomerular filtration rate; HbA1c=hemoglobin A1c; DR=diabetic retinopathy

from these can be used as a risk stratification tool whether kidney biopsy should be performed or not.

The majority of the present study cases had kidney biopsies due to sudden onset of proteinuria or nephrotic syndrome or rapid eGFR decline. This conformed with standard indications in the KDOQI guideline[4]. Unfortunately, the results showed only around half (53%) of the study population had any type of NDKD with either NDKD alone or DN+NDKD, and the remainder had DN alone. This may mean the kidney biopsy was unnecessarily performed in those cases and atypical features can be found in DN. Previous kidney biopsy studies reported varying prevalence of NDKD. In a literature review, Kanodia et al[1] found the percentage of NDKD ranged from 45% to 75%. Sharma et al[3] reviewed 620 biopsies in patients with diabetes and noted 63% had NDKD. Because of this moderate yield in NDKD detection, there is room for a diagnostic tool to differentiate T2DM patients with low or high probability of NDKD.

Previous research has reported some predictors associated with NDKD. Similar to the present study findings, the absence of DR was the strongest predictor of NDKD in many studies[2,5,6-9,17,18]. In other words, when DR is present, it is a suggestive of DN in T2DM, because both are microvascular complications. Longer duration of DM is inversely associated with NDKD. Dong et al[8] found that a DM history of less than or equal to five years had aOR of 4.6 (95% CI 1.7 to 12.5), Kritmetapak et al[7] reported a duration of DM of more than eight years with an aOR of 0.15 (95% CI 0.04 to 0.49), and finally, Yang et al[9] showed a duration of DM of less than ten years and more than five years had aOR of 0.06 (95% CI 0.97 to 0.75). In the authors' opinion, the exact duration of T2DM

seems difficult to obtain. Therefore, the authors used a cutoff of less than 10 years for simplicity and found significant associations in the univariable model but not within the multivariable model. This latter phenomenon may be due to low power. Higher renal function was found to be a significant predictor in a recent study[9], showing eGFR greater than or equal to 90 mL/minute/1.73 m² had aOR of 6.38 (95% CI 1.58 to 25.7). Although, the present study similarly found higher eGFR in NDKD, some etiologies of NDKD, such as acute tubular necrosis, acute interstitial nephritis, or thrombotic microangiopathy had low eGFR. High HbA1c or fasting blood sugar were reported in a few studies[5,7]. Unlike previous reports[6,9,18], the authors could not find any association of proteinuria levels with NDKD as most of the present study population already had macroalbuminuria.

The present study may be the first to combine predictors into a comprehensive risk stratification score. The present model had a good discrimination (AUROC 0.75) and calibration (Hosmer-Lemeshow test, p=0.29). For clinical implications, the authors now proposed an algorithm by categorizing the clinical prediction scores into three groups, low probability, intermediate probability, and high probability of NDKD. In the low probability group, patients may defer kidney biopsy (Figure 2). This could be useful for deciding kidney biopsy and prevent patient discomfort and surgical complications. However, with intermediate and high probability, a kidney biopsy is still suggested for definite diagnosis of NDKD.

The authors must still point out that there are some essential limitations to consider in the present work here. First, the small sample size is likely to have affected the statistical power, potentially creating a risk of overfitting and optimism bias. The authors attempted to manage this by choosing predictors from previous studies and using a p-value of 0.20 to select predictors into the multivariable analysis, without backward elimination if the predictors were not statistically significant. Internal validation was done with bootstrapping to adjust the developed model for optimism. Second, the inherent nature of retrospective data collection can affect data quality in the verification of outcomes, missingness and bias due to patient selection for kidney biopsy. As around 5% of the present data was missing for the essential predictors, complete-case analysis was used.

Conclusion

In conclusion, a clinical prediction score for NDKD is a useful risk stratification tool for kidney biopsy in T2DM patients with atypical presentations. Using multiple predictors as opposed to a sole one appeared to improve the predictive ability. Hopefully, this kind of score can lead to the deferment of unnecessary kidney biopsy. It would be interesting to apply this prediction score in other populations at other centers to observe if the scores could ameliorate its external validity.

What is already known on this topic?

NDKD can occur in patients with type 2 diabetes mellitus and usually require a kidney biopsy for definite diagnosis. Previous studies found that some predictors were associated with NDKD. However, in clinical practice, these predictors can be found simultaneously in each patient, and it is difficult to interpret.

What this study adds?

This study combined relevant clinical predictors, such as duration of DM, eGFR, HbA1c, and absence of DR, into a clinical prediction score, which could predict a probability of NDKD. The scores were categorized into three groups, low, intermediate, and high probability. These scores may guide clinicians to make a decision whether kidney biopsy is required if the result is in the higher score or can be deferred if the result is in the lower score to avoid the risk of complications of the invasive procedure.

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Conflicts of interest

Authors declare no conflict of interests.

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