ORIGINAL ARTICLE

LASSO-derived nomogram predicting new-onset diabetes mellitus in patients with kidney disease receiving immunosuppressive drugs

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Abstract
What is known and objective: Patients with kidney disease receiving immunosuppressive drugs (ISDs) (tacrolimus, cyclosporine and glucocorticoids) have a high risk of developing new-onset diabetes mellitus (NODM). We aimed to establish a precise and convenient model for predicting NODM in patients receiving immunosuppressive drugs.

Methods: This retrospective study recruited 1883 patients receiving ISDs between January 2010 and October 2018. The occurrence of NODM was the primary endpoint. The patients were randomly divided into training (n = 1318) and validation cohorts (n = 565) at a 7:3 ratio. A nomogram was established based on a least absolute shrinkage and selection operator (LASSO)-derived logistic regression model. The nomogram’s discrimination and calibration abilities were evaluated in both cohorts using the Hosmer-Lemeshow test and calibration curves. Decision curve analysis (DCA) was used to evaluate the net benefit of the predictive efficacy.

Results and discussion: Amongst the 1883 patients with kidney disease receiving immunosuppressive drugs, 375 (28.5%) and 169 (29.9%) developed NODM in the training (n = 1318) and validation cohorts (n = 565), respectively. Nine clinic predictors were included in this LASSO-derived nomogram, which is easy to be operated clinically. The discriminative ability, determined by the area under the receiver operating characteristic curve (AUC), was 0.816 (95% confidence interval [CI] 0.790–0.841) and 0.831 (95%CI 0.796–0.867) in the training and validation cohorts, respectively. Calibration was confirmed with the Hosmer-Lemeshow test in the training and validation cohorts (p = 0.238, p = 0.751, respectively).

What is new and conclusion: Nearly one-third of patients with kidney disease receiving immunosuppressive drugs developed NODM. The nomogram established in this
study may aid in predicting the occurrence of NODM in patients with kidney disease receiving immunosuppressive drugs.

**KEYWORDS**

immunosuppressive drugs, LASSO, new-onset diabetes mellitus, nomogram, risk model

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1 | WHAT IS KNOWN AND OBJECTIVE

The prevalence of kidney disease and mortality associated with it have gradually increased since 1990, and kidney disease is now recognized as a major and growing public health concern worldwide. First-line immunosuppressive agents, such as tacrolimus, cyclosporine and glucocorticoids, are widely used and have proven successful in the treatment of kidney diseases. However, immunosuppressive drug (ISD) therapy is associated with adverse effects, such as hyperglycemia. In general, the administration of corticosteroids and calcineurin inhibitors (CNIs) is considered the predominant factor associated with the development of post-transplant diabetes mellitus. A growing body of evidence has indicated potential associations between ISD use and increased risk of incident new-onset diabetes mellitus (NODM). In addition, studies have documented that the prognosis and survival are poorer amongst patients with NODM than amongst those without NODM.

Early evaluation of patients who are likely to develop NODM may aid in guiding adjuvant therapy, thereby improving outcomes. Of note, findings regarding the incidence of and risk factors for the development of NODM in patients treated with ISDs have been heterogeneous. More accurate predictive tools are required, given the controversial conclusions of previous models. These controversial conclusions likely occurred due to the small sample sizes or a focus on specific kidney diseases, such as renal transplantation and idiopathic membranous nephropathy.

The least absolute shrinkage and selection operator (LASSO) regression, which is an advanced variable selection algorithm for multicollinear or high-dimensional data, has proven to be the best algorithm for reducing multicollinearity amongst variables. It is especially suitable for dealing with an enormous number of clinical factors and avoiding over-fitting. Nomograms are simple statistical visual tools that can be used as regression algorithms to predict the probability of a given outcome. They have become increasingly popular given their benefits of easy visualization and understandability. However, nomograms have rarely been used to predict the development of NODM in patients with kidney disease. Accordingly, the present study aimed to establish a LASSO-based nomogram for precisely and conveniently identifying patients receiving ISDs who are likely to develop NODM.

2 | METHODS

2.1 | Data sources and processing

Demographic data, medical histories, clinical diagnoses, laboratory data, and medical data, which were generally found or tested in those patients, were extracted from the hospital's electronic medical records system.

A total of 2954 patients treated for kidney disease using ISDs (tacrolimus, cyclosporine and glucocorticoids) between January 2010 and October 2018 were enrolled in this retrospective study. Those with a history of diabetes mellitus (n = 124) and abnormal baseline fasting blood glucose (FBG) level of >7 mmol/L (n = 86), those with missing key parameters such as FBG after ISD therapy or body mass index (BMI) (n = 486), and those with a follow-up duration of <4 weeks (n = 375) were excluded from the study. Finally, a total of 1883 patients were included in the study. Patients were divided into the training (n = 1318) and validation (n = 565) cohorts at a ratio of 7:3 using R software.

2.2 | Statement of human and animal rights

The study was approved by the Ethics Committee of Zhejiang Provincial People's Hospital (2021QT184). The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013).

2.3 | Informed consent

The need for informed consent was waived owing to the retrospective study design.

2.4 | Definitions

To receive a diagnosis of NODM, patients must have had no history of diabetes or diabetes-related symptoms, as well as normal FBG before ISD treatment. NODM was defined as follows: persistence of abnormally elevated FBG or elevated random blood glucose during the 1 year after beginning ISD treatment, based on the American Diabetes Association guidelines. These guidelines included symptoms of diabetes with a rapid plasma glucose level ≥ 11.1 mmol/L, a fasting plasma glucose level ≥ 7.0 mmol/L, a 2-h plasma glucose level ≥ 11.1 mmol/L during an oral glucose tolerance test, or plasma haemoglobin (Hb) A1c ≥ 6.5%.

2.5 | Statistical analyses

The baseline characteristics of the two cohorts were described using counts and percentages for categorical variables and medians with
interquartile ranges for continuous variables. Differences between
groups were examined using chi-square tests or Fisher’s exact tests
for categorical variables and t-tests or Wilcoxon tests for continuous
variables, depending on the nature of the distribution.

Imputation was conducted if missing values were <20%. We used
predictive mean matching to impute numeric features, and logistic
regression to impute binary variables. We used LASSO regression to
minimize the potential collinearity of over-fitting variables and vari-
ables measured from the same patient. The R package “glmnet”
(R Foundation) was used to perform the LASSO regression. This is a
logistic regression model that penalizes the absolute size of the coe-
ficients of a regression model based on the value of λ. With larger pen-
alties, the estimates of weaker factors shrink towards zero, such that
only the strongest predictors remain in the model. The most predic-
tive covariates were selected based on the λ (λ = Lambda.1se). Subse-
quently, variables identified via the LASSO regression analysis were
entered into logistic regression models by using forward stepwise
(Likelihood Ratio), and those that were consistently statistically signifi-
cant were used to construct the risk model. The independent variables
were checked for collinearity using the variance inflation factor (VIF)
and tolerance test.

A nomogram was developed based on the final model. Validations
were implemented to evaluate the predictive performance of the
derived nomogram in terms of discrimination and calibration. For
independent validation, to account for the potential discrepancy
between the training and validation datasets, calibration plots were
created for the original and recalibrated nomograms. Discrimination
was assessed using the receiver operating characteristic (ROC) curve
and the area under the curve (AUC). Calibration was assessed by com-
paring the observed NODM rates with predictions from the final
model. Decision curve analysis (DCA) was performed to evaluate the
net clinical benefits. All statistical analyses were performed using R
software, version 3.6.2 (R Foundation for Statistical Computing), and a
two-sided p-value of <0.05 was considered statistically significant for
all tests.

3 | RESULTS AND DISCUSSION

3.1 | Baseline characteristics of the training and validation cohorts

We analysed the data from 1318 patients in the training cohort
(median age: 56 years), which included 588 (44.6%) men. Thirty-one
(2.4%) patients had a family history of diabetes, whilst 246 (18.7%)
had hypertension. The median FBG level was 4.88 mmol/L. Amongst
(2.4%) patients had a family history of diabetes, whilst 246 (18.7%)
(375/1318) and 29.9% (169/565) in the training and validation
cohorts, respectively. Table 1 shows the comparison of the
demographic and clinical variables between the training and validation
cohorts. There were no statistically significant differences between the
two cohorts.

3.2 | Predictor selection and identification

Fifty variables measured at baseline (i.e., hospital admission) (Table 1)
were included in the LASSO regression analysis. After LASSO regres-
sion selection (Figure 1), the following 20 variables remained signifi-
cant predictors of NODM, including clinical features, ISD therapy, and
blood test results: sex, age, tacrolimus use, duration of tacrolimus use,
cyclosporine use, number of intravenous glucocorticoid treatments at
a dosage of 500 mg, intravenous glucocorticoid treatment at a dosage
of 40 mg, duration of intravenous glucocorticoid treatment at a dosa-
age of 40 mg, hypertension, FBG, haematocrit, Hb, serum creatine,
uric acid, high sensitivity C-reactive protein, white blood cell count,
red cell distribution width, diagnosis of lupus nephritis, diagnosis of
acute kidney injury (AKI) and diagnosis of other kidney diseases (renal
transplant recipients, interstitial nephritis and other glomerular dis-
eases of uncertain pathologic type).

These 20 variables were included in the logistic regression model,
and nine variables were found to be significant independent predic-
tors of NODM. These variables included sex (female) (odds ratio [OR],
0.659; 95% confidence interval [CI], 0.494–0.879; p = 0.005), age
(OR, 1.029; 95% CI, 1.021–1.037; p < 0.001), tacrolimus use (OR,
2.986; 95% CI, 1.973–4.520; p < 0.001), cyclosporine use (OR, 2.571;
95% CI, 1.488–4.440; p = 0.001), number of intravenous glucocorti-
coid treatments at a dosage of 500 mg (OR, 1.180; 95% CI, 1.068–
1.304; p = 0.001), intravenous glucocorticoid treatment at a dosage
of 40 mg (OR, 3.545; 95% CI, 2.364–5.137; p < 0.001), duration of
intravenous glucocorticoid treatment at a dosage of 40 mg (OR,
1.019; 95% CI, 1.008–1.030; p < 0.001), FBG (OR, 1.295; 95% CI,
1.091–1.536; p = 0.003) and diagnosis of AKI (OR, 8.216; 95% CI,
5.321–12.678; p < 0.001) (Table 2). Furthermore, the tolerance was
>0.1, and VIF was significantly <10 for the training set, indicating no
collinearity amongst the independent variables (Table S1).

3.3 | Nomogram construction

The risk of NODM was calculated using the following multivariate logistic
regression equation: \( \ln(p/1 - p) = -0.417 \times Sex + 0.029 \times Age +
1.094 \times Tacrolimus \ use + 0.944 \times Cyclosporine \ use + 0.166 \times GC
500 mg + 1.266 \times GC 40 mg + 0.019 \times GC 40 mg \ Time +
0.258 \times FBG + 2.106 \times Diagnosis \ AKI - 4.930. \)
In the equation, \( p \) represents the probability of NODM.

A prognostic nomogram for patients receiving ISD therapy that
would likely progress to NODM was constructed using the multivari-
ate logistic regression results (Figure 2). Points were assigned to the
identified factors according to the absolute maximum beta value
based on the logistic regression model, given that the units are differ-
ent for the continuous (age, number of intravenous glucocorticoid
TABLE 1  Comparison of variable characteristics between training cohort and validation cohort

| Variables                        | Training cohort | Validation cohort | p-Value |
|----------------------------------|-----------------|-------------------|---------|
| No.                              | 1318            | 565               |         |
| Age (years)                      | 56 (38–69)      | 56 (41–70)        | 0.370   |
| BMI                              | 21.8 (19.5–24.5)| 22.0 (19.6–24.3) | 0.841   |
| Gender (male) n (%)              | 588 (44.6)      | 239 (42.3)        | 0.354   |
| Smoking habit n (%)              | 275 (20.9)      | 99 (17.5)         | 0.178   |
| Drinking habit n (%)             | 191 (14.5)      | 61 (10.8)         | 0.083   |
| DM family history n (%)          | 31 (2.4)        | 15 (2.7)          | 0.696   |
| Hypertension n (%)               | 246 (18.7)      | 106 (18.8)        | 0.961   |
| Cardiovascular disease n (%)     | 22 (1.7)        | 10 (1.8)          | 0.877   |
| Fasting blood-glucose, mmol/L    | 4.88 (4.43–5.49)| 4.83 (4.47–5.47) | 0.993   |
| Haematocrit                      | 0.360 (0.306–0.410)| 0.362 (0.305–0.405)| 0.995   |
| Haemoglobin, g/L                 | 118 (99–136)    | 119 (99.4–135)    | 0.901   |
| Albumin, g/L                     | 33.3 (27.0–39)  | 33.8 (27.95–39.3) | 0.117   |
| Creatinine, μmol/L               | 82.4 (66.1–127.5)| 80.3 (67.2–125)  | 0.954   |
| LDLC, mmol/L                     | 2.71 (1.99–3.55)| 2.65 (1.94–3.55)  | 0.258   |
| Triglyceride, mmol/L             | 1.49 (1.04–2.18)| 1.47 (1.09–2.22)  | 0.871   |
| Uric acid, μmol/L                | 336 (257–437)   | 340 (266–437)     | 0.512   |
| HDLC                             | 1.11 (0.84–1.46)| 1.09 (0.82–1.47)  | 0.615   |
| hsCRP                            | 7.8 (1.9–31.95) | 7.2 (1.9–31.95)   | 0.818   |
| White blood cell count, × 10⁹/L  | 6.83 (4.9–9.61) | 6.90 (4.83–10.05) | 0.668   |
| Lymphocyte count, × 10⁹/L        | 1.40 (0.93–2.01)| 1.41 (0.99–2.06)  | 0.382   |
| Lymphocyte %                     | 22.04 (14.6–30.2)| 22.70 (14.9–29.6)| 0.511   |
| RDW-SD                           | 45.1 (41.4–48.2)| 45.2 (41.8–48.25)| 0.565   |
| RDW-CV                           | 13.7 (12.8–15.1)| 13.7 (12.8–14.9)  | 0.792   |
| Neutrophil cell count, × 10⁹/L   | 4.70 (3.14–6.87)| 4.77 (3.12–7.19)  | 0.665   |
| Neutrophil cell %                | 70.2 (61.4–78.4)| 69.60 (61.2–78.5) | 0.808   |
| FK506, mean (SD) [range] ng/L    | 0.58 (2.2) [0–22]| 0.61 (2.3) [0–20.5]| 0.847   |
| Tacrolimus n (%)                 | 196 (14.9)      | 88 (15.6)         | 0.696   |
| Duration of tacrolimus, mean (SD) [range] | 3 (11) [0–242]| 3 (10) [0–88] | 0.760   |
| Ciclosporin n (%)                | 83 (6.3)        | 26 (4.6)          | 0.149   |
| Duration of ciclosporin, mean (SD) [range] | 2 (9) [0–170]| 1 (5) [0–59] | 0.300   |
| GC 500 mg n (%)                  | 130 (9.9)       | 47 (8.3)          | 0.292   |
| GC 500 mg time mean (SD) [range] | 0 (1) [0–19]| 0 (1) [0–7] | 0.138   |
| GC 40 mg n (%)                   | 891 (67.6)      | 390 (69)          | 0.544   |
| GC 40 mg time (day)              | 4 (0–11)        | 4 (0–12)          | 0.295   |
| GCoral n (%)                     | 1011 (76.7)     | 425 (75.2)        | 0.487   |
| GCoral time (day)                | 4 (1–13)        | 4 (1–13)          | 0.909   |

Diagnosis

|                        | Training cohort | Validation cohort | p-Value |
|------------------------|-----------------|-------------------|---------|
| Nephrotic syndrome     | 278 (21.1)      | 107 (18.9)        | 0.288   |
| Idiopathic membranous nephropathy | 109 (8.3) | 48 (8.5) | 0.871   |
| IgA nephropathy        | 83 (6.3)        | 44 (7.8)          | 0.237   |
| Minimal change disease | 8 (0.6)         | 1 (0.2)           | 0.294   |
| Mesangial proliferative glomerular nephritis | 10 (0.8) | 3 (0.5) | 0.584   |
| Anca associated systemic vasculitis | 76 (5.8) | 41 (7.3) | 0.220   |
| Lupus nephritis        | 271 (20.6)      | 100 (17.7)        | 0.152   |
TABLE 1 (Continued)

| Variables                              | Training cohort | Validation cohort | p-Value |
|----------------------------------------|-----------------|-------------------|---------|
| Sjogren’s syndrome                     | 106 (8)         | 45 (8)            | 0.955   |
| Rheumatoid arthritis                   | 117 (8.9)       | 58 (10.3)         | 0.342   |
| Henoch-schonlein purpura nephritis     | 30 (2.3)        | 11 (1.9)          | 0.654   |
| Renal transplant recipients            | 17 (1.3)        | 2 (0.4)           | 0.063   |
| Acute kidney injury                    | 153 (11.6)      | 67 (11.9)         | 0.877   |
| Other kidney disease                   | 188 (14.3)      | 91 (16.1)         | 0.302   |
| Follow up time (day)                   | 183 (53–513)    | 144 (56–409)      | 0.187   |
| NODM                                   |                 |                   |         |
| Yes                                    | 375 (28.5)      | 169 (29.9)        | 0.522   |
| No                                     | 943 (71.5)      | 396 (70.1)        |         |

Abbreviations: BMI, body mass index; DM family History, diabetes mellitus family history; FK506, minimum concentration of tacrolimus; GC 40 mg, intravenous glucocorticoid of 40 mg dosage form use; GC 40 mg time, duration intravenous glucocorticoid of 40 mg dosage form; GC 500 mg, intravenous glucocorticoid of 500 mg dosage form; GC 500 mg time, numbers of intravenous glucocorticoid of 500 mg dosage form; GCoral, oral dosage form of glucocorticoids; GCoral time, duration of oral dosage form of glucocorticoids; HDLC, high density lipoprotein cholesterol; hsCRP, high sensitivity C reactive protein; LDLc, low-density lipoprotein cholesterol; NODM, new onset diabetes mellitus; RDW-CV, red blood cell distribution width—coefficient of variation; RDW-SD, red blood cell distribution width—standard deviation.

FIGURE 1 Feature selection using the least absolute shrinkage and selection operator (LASSO) binary logistic regression model. (A) LASSO coefficient profiles of the 50 baseline features. (B) Tuning parameter (λ) selection in the LASSO model used 10-fold cross-testing via minimum criteria.

treatments at a dosage of 500 mg, intravenous glucocorticoid treatment at a dosage of 40 mg, duration of intravenous glucocorticoid treatment at a dosage of 40 mg and FBG) and categorical (sex, tacrolimus use, cyclosporine use and diagnosis of AKI) predictors. As shown in the nomogram, patients with the following characteristics were more likely to progress to NODM: male sex, older in age, treatment with tacrolimus, treatment with cyclosporine, more frequent intravenous glucocorticoid treatments at a dosage of 500 mg, intravenous glucocorticoid treatment at a dosage of 40 mg, longer duration of intravenous glucocorticoid treatment at a dosage of 40 mg, higher FBG and diagnosis of AKI. The longer the length of the line was, the larger the impact of those factors in developing NODM might have. Summing all points led to a total score. Locating the total score on the nomogram scale, the risk of progressing to NODM could be determined at patient presentation.

A hypothetical case illustrating our nomogram usage is presented in Figure S1. If a 60-year-old male patient with an FBG of 5.5 mmol/L is treated with oral tacrolimus, in combination with intravenous glucocorticoid 40 mg per day for 8 weeks, the total points add up to 190 and the corresponding risk of NODM is approximately 78%, which indicates a high predicted probability of NODM for this patient.
3.4 | Nomogram validation

We performed independent validation of our nomogram in the validation cohort (Figure 3B), which yielded an AUC value of 0.831 (95% CI: 0.796–0.867). The calibration curve revealed excellent concordance between the nomogram prediction and actual observation of NODM. The Hosmer–Lemeshow test yielded p-values of 0.238 and 0.751 in the training and validation cohorts, respectively (Figure 4). We further plotted the DCA curves of the training and validation cohorts to assess the clinical utility of our risk model. Our nomogram showed a net benefit across a wide scale of threshold probabilities for the prediction of NODM, regardless of the training cohort or the validation cohort (Figure 5).

3.5 | Discussion

In the present study, we developed and validated a nomogram for predicting NODM in patients with kidney disease receiving ISDs based on a combination of variables. This predictive nomogram exhibited satisfactory accuracy based on AUCs (>0.81) in both the training and validation cohorts. In addition, high discriminative and calibration abilities were confirmed in both the training and validation cohorts. To the best of our knowledge, this is the first LASSO-derived risk model for NODM in patients with kidney disease receiving ISD. In practice, our easy-to-use nomogram may aid in clinical decision-making, as the required data are generally easily accessible in a clinical setting. If the patient's estimated risk for NODM is low, the clinicians may choose to perform continuous

### TABLE 2

LASSO-derived multivariable logistic regression model for predicting NODM in training cohort (n = 1318)

| Variables            | OR   | Odds ratio (95% CI) | p Value |
|----------------------|------|---------------------|---------|
| Female               | 0.659| 0.494–0.879         | 0.005   |
| Age (years)          | 1.029| 1.021–1.037         | <0.001  |
| Tacrolimus           | 2.986| 1.973–4.520         | <0.001  |
| Ciclosporine         | 2.571| 1.488–4.440         | 0.001   |
| GC 500 mg time (No.)| 1.18 | 1.068–1.304         | 0.001   |
| GC 40 mg             | 3.545| 2.364–5.137         | <0.001  |
| GC 40 mg time (day)  | 1.019| 1.008–1.030         | <0.001  |
| FBG (mmol/L)         | 1.295| 1.091–1.536         | 0.003   |
| Diagnosis AKI        | 8.216| 5.321–12.678        | <0.001  |

Abbreviations: Diagnosis AKI, be diagnosed as acute kidney injury; FBG, fasting blood-glucose; GC 40 mg, intravenous glucocorticoid of 40 mg dosage form use; GC 40 mg time, duration intravenous glucocorticoid of 40 mg dosage form; GC 500 mg time, numbers of intravenous glucocorticoid of 500 mg dosage form.
monitoring, whereas high-risk estimates may support a change in the treatment regimen.

Our study demonstrated that the morbidity of NODM in patients with kidney disease receiving ISD was high, with rates of 28.5% in the training cohort and 29.9% in the validation cohort. These rates are lower than those reported in our previous small-scale study involving patients with idiopathic membranous nephropathy undergoing tacrolimus and low-dose corticosteroid therapy. The difference may be explained by the prior diabetogenic effects of tacrolimus, which may reduce insulin secretion due to islet cell necrosis and increase insulin resistance.

In the model derivation, we used the LASSO to select the predictors. LASSO regularization is a statistical approach to address overfitting and to perform a variable selection that has been widely used in many types of predictive models and machine learning algorithms. The final nomogram model was developed based on the following nine risk factors identified in the multivariate analysis: sex, age, tacrolimus use, cyclosporine use, number of intravenous glucocorticoid treatments at a dosage of 500 mg, intravenous glucocorticoid treatment at a dosage of 40 mg, duration of intravenous glucocorticoid treatment at a dosage of 40 mg, FBG level and diagnosis of AKI.
Our analysis revealed that the usage of glucocorticoids, especially high-dosage intravenous glucocorticoids, played an important role in our predictive model, which is consistent with previous research. Tacrolimus and cyclosporine are widely used in patients with kidney disease due to their strong immunosuppressive effects, and previous studies have documented their diabetogenic effects. Similar findings were observed in the present study. Multiple studies have indicated that age, current smoking, BMI, family history of diabetes, history of hypertension and tacrolimus use are risk factors for NODM in patients taking ISDs following renal transplantation and for glomerular disease. Our previous study demonstrated that age is an independent risk factor for NODM in patients with idiopathic membranous nephropathy treated with ISDs. Glucose tolerance progressively declines with age, which may be caused by the shortening of telomeres in β and α cells and by age-related changes in DNA methylation in human islet cells. These two effects may explain the main study finding that older age increased the risk of developing NODM. Surprisingly, FBG within the normal range was a risk factor for NODM. One study recommended that we should pay more attention to patients with baseline glycosylated haemoglobin in the non-diabetic range that reaches >5.65% during chronic kidney disease treatment with CNIs. Although previous studies have not identified AKI as a major risk factor for NODM, AKI was extremely important in our risk model. Of the various kidney diseases included in this study, NODM was most frequently associated with AKI. Patients with renal diseases involving AKI, such as lupus nephropathy, antineutrophil cytoplasmic antibody-associated vasculitis, and nephrotic syndrome, tend to receive higher doses and/or longer durations of glucocorticoid therapy.

There are some limitations to this study. First, this study was conducted using the database of a single centre in China, which may preclude the generalization of this nomogram to patients in the rest of the world. Thus, further studies are required to validate our model using data from multiple centres. Second, some patients with missing data were removed from the analysis, as data were not considered to be missing at random, leading to some selection bias. However, LASSO was used to ensure the accuracy of the model and to prevent over-fitting. Lastly, because this was a retrospective analysis, some cases were lost to follow-up, which may have impacted the accuracy of the model. Prospective studies are required to verify and optimize the model.

WHAT IS NEW AND CONCLUSION

In this study, we developed a predictive nomogram to estimate the risk of developing NODM amongst patients with kidney disease receiving ISDs. Estimating the risk of NODM may aid in identifying patients who are and are not likely to develop NODM, thus supporting appropriate treatment and optimizing ISD therapy in patients with kidney disease. The incidence of NODM in these patients was high, which requires the common attention of nephrologists, endocrinologists and community physicians. Over the next years, we look forward to achieve better management of this subset of patients through the multi-disciplinary cooperation of experts in nephrology and endocrinology.

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CONFLICT OF INTEREST
The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT
The datasets of this study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

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