A differential diagnostic model of diabetic nephropathy and non-diabetic renal diseases

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Abstract

Background. Renal diseases in diabetes include diabetic nephropathies (DN) and non-diabetic renal diseases (NDRD). The clinical differentiation between these two categories is usually not so clear and effective. This study aims to develop a quantified differential diagnostic model.

Methods. We consecutively screened the diabetic patients with overt proteinuria but no severe renal failure for kidney biopsy from 1993 to 2003. The finally enrolled 110 patients were divided into two groups according to pathological features (60 in DN group and 50 in NDRD group). Clinical and laboratory data were compared between two groups. Then a diagnostic model was developed based on the logistic regression analysis.

Results. Forty-six percent of patients were NDRD including a variety of pathological types. Many differences between DN and NDRD were found by comparison of the clinical indices. In the final logistic regression analysis, only diabetes duration (Dm), systolic blood pressure (Bp), HbA1c (Gh), haematuria (Hu) and diabetic retinopathy (Dr) showed statistical significance. Based on the logistic regression model: π = exp(−13.5922 + 0.0371Dm + 0.3224Gh + 0.0395Bp + 2.9613Dr)/[1 + exp(−13.5922 + 0.0371Dm + 0.3224Gh + 0.0395Bp + 2.9613Dr)], PDN was the probability of DN diagnosis (PDN ≥ 0.5 as DN, PDN < 0.5 as NDRD). Validation tests showed that this model had good sensitivity (90%) and specificity (92%).

Conclusions. This diagnostic model may be helpful to clinical differentiation of DN and NDRD in type 2 diabetic patients with overt proteinuria.

Keywords: diabetic nephropathies; differential diagnosis; discriminant analysis; type 2 diabetes mellitus

Introduction

The incidence and prevalence of diabetes mellitus (DM) are increasing. In the United States, the prevalence was about 8%. In 2005, 1.5 million new cases of diabetes were diagnosed in people aged 20 years or older [1]. The situation is similar in other countries. Nowadays, altogether 120 million people are diabetic in the world and the number will triple in 30 years. The diabetes-related medical cost is increasing [2]. DM has become an enormous social problem. Accordingly, the prevalence of diabetic nephropathy (DN) is also increasing. It has become the leading cause of end-stage renal diseases (ESRD) in developed countries. By USRDS reports [3], the number of incident patients with diabetes as their primary cause of renal failure will continue to increase though the growth rate has slowed a little bit. In China, it is turning out to be a major cause of ESRD.

However, DN is not the only renal disease in diabetes. Many of non-diabetic renal diseases (NDRD) have been uncovered by renal biopsy. It is usually believed that DN is hard to reverse. But some NDRD, such as mesangial proliferative glomerulonephritis, IgA nephropathy and membranous nephropathy, are often treatable, even remittable. The therapy and prognosis of DN and NDRD are quite different, so the differential diagnosis is of considerable importance. Previous literature has covered much of the differentiation that included the diabetes duration, retinopathy, haematuria and other indices. But the results were diverse, partly because of the deficit of a quantified standard, and partly because they are not practicable enough for physicians with less experience.

The kidney biopsy could discriminate DN from NDRD, but it is invasive and not suitable for every patient, what kind of patients should we perform a biopsy on? The point in question, therefore, was what kind of patients criteria different kidney centres, and the real frequency of NDRD is not clear due to the diversified criteria for biopsy among different kidney centers, the-real frequency [4,5]. The present study is designed to perform kidney biopsies on each diabetic patient with overt proteinuria and aims to develop a differential diagnostic model by comparison between DN
and NDRD. Consequently, a quantified probability can be calculated using this model, and a more practicable differential diagnosis could be made.

Subjects and methods

According to the research protocol approved by the Ethics Committee of the Chinese PLA General Hospital, we consecutively screened patients aged 18–70 years for this study at the Nephrology Department of Chinese PLA General Hospital. The inclusion criteria were as follows: diagnosed as type 2 DM; with persistent overt proteinuria (defined as urinary albumin excretion ≥300 mg/24 h or urinary protein excretion ≥500 mg/24 h by at least two tests without evidence of urinary tract infection); with serum creatinine <442 μmol/L; willing to be hospitalized and undergo a kidney biopsy. From January 1993 to December 2003, 113 type 2 diabetic patients with persistent overt proteinuria underwent a kidney biopsy.

All the biopsied patients had signed the informed consent previously. Tissue was separated and allocated for immunofluorescence microscopy (IF), light microscopy (LM) and electron microscopy (EM). Tissue for IF was surrounded with OCT compound and frozen, then stained with fluorescein-tagged antibodies against IgG, IgA, IgM, complements C3, C4, C1q, fibrin-related antigen and HBV-associated antigens. Tissue for LM was placed into formalin and dehydrated, then placed in a paraffin block and sections were stained by haematoyxin and eosin, periodic acid-Schiff, silver methenamine, and Masson trichrome. Tissue for EM was placed in glutaraldehyde and sent to Electron Microscope Centre. The tissue was examined by at least two pathology experts together with another two nephrologists; then the pathological diagnosis was determined.

According to pathological changes, the patients were divided into two groups (DN group and NDRD group). In fact, there were three regimes: DN alone, NDRD and an overlapped type. Most of them were diagnosed unequivocally. Marked morphological changes in LM, including diffuse mesangial expansion with predominance of increased mesangial matrix, Kimmelstiel–Wilson nodular lesions, hyaline exudative lesions and glomerular basement membrane (GBM) thickening, were considered to be related to DN [6]. Glomerulopathies not related to diabetes usually have some unique features. Special patterns of antibody deposition in IF (e.g. IgA deposition, Predominantly in mesangial region, immuno-complex sub-epithelial deposition, etc.) and characteristics of glomerular lesions in LM (crescentic, double contour, etc.) which can often provide enough evidence for diagnosis of NDRD. In some cases, LM plus IF cannot provide enough information. For example, when nearly normal glomerular structure or mild alterations without special immune deposits were presented, EM was investigated. As a result of the investigation, we may find mild to moderate thickening of GBM or effacement of the podocyte foot processes as features of the diabetic glomerulopathy or minimal change disease, or we may find nothing special; in this case minor glomerular abnormalities were diagnosed. Without EM results, these cases could not be defined precisely. Among the 113 patients in this study, 60 cases were diagnosed as DN, 50 were NDRD, 2 were diagnosed as overlapped DN with NDRD and only 1 showed ambiguous pathological changes (no EM results). In order to develop a separation tool, we omitted the overlapped group and equivocal case. Thus, 110 patients were finally enrolled.

Clinical and laboratory data of each patient were analysed. We compared clinical features and laboratory test results between the groups.

The descriptive statistics were presented as mean ± SD for measurement data and percentage for enumeration count data. Differences between groups were assessed by ANOVA for normally distributed measurement data, Wilcoxon’s test for non-normally distributed measurement data and the chi-square test for enumeration data. Univariate logistic regression analysis was used to screen factors relating to the diagnosis, and by multivariate logistic regression analysis (stepwise forward, \( P_{c} \) 0.05, \( P_{r} \) 0.06; the \( P_{c} \) option is the probability of entering a variable; the \( P_{r} \) option is the probability of removing a variable), the final significant factors were included in the differential diagnostic model. This was based on the logistic regression model: \( \pi = e^{\beta x} / (1 + e^{\beta x}) \) [7]. \( \pi \) is probability, \( e \) is mathematical constant \((e = 2.71828...\) ), \( z \) is linear combination of \( x \) and \( \beta \), i.e., \( z = \alpha + \beta_{1}x_{1} + \beta_{2}x_{2} + \beta_{3}x_{3} + ... + \beta_{q}x_{q} \), where \( \alpha \) is constant, \( x \) is variable, \( \beta \) is the estimator; then the equation turns into the following: \( \pi = \exp(\alpha + \beta_{1}x_{1} + \beta_{2}x_{2} + \beta_{3}x_{3} + ... + \beta_{q}x_{q}) / [1 + \exp(\alpha + \beta_{1}x_{1} + \beta_{2}x_{2} + \beta_{3}x_{3} + ... + \beta_{q}x_{q})] \). In our diagnostic model, \( x \) is the clinical predictor, \( \beta \) is the estimator and \( \pi \) is the probability of DN diagnosis.

We calculated the \( \pi \)-value of each patient; if \( \pi \geq 0.5 \), the patient should be considered as DN, while if \( \pi < 0.5 \), the preliminary diagnosis should be NDRD. Upon these calculations, we got the sensitivity and specificity at a certain cutoff value of 0.5. Sensitivity = true positive/(true positive + false negative); specificity = true negative/(false negative + true positive). Changing the cutoff level of \( \pi \) (0.5 here) caused alteration of the corresponding sensitivity and specificity. Then a receiver operating characteristic (ROC) curve was made to show the variations of sensitivity and specificity by different cutoff levels. The closer the curve is to the diagonal, i.e., the closer the area under the curve (AUC) is to 0.5, the worse the model. In contrast, the closer the AUC is to 1.0, the better the model. Finally, we conducted an internal (back-substitution) and further (by a validation cohort of 21 patients) validation test of the model. All these tests were performed with STATA/SE 8.0 for Windows.

Results

Demographic profile

Mean age (at biopsy) was 46.3 ± 11.8 years. Sex ratio was 2.3:1 (male: female). Median diabetes duration (from diagnosis of diabetes to kidney biopsy) was 59.8 months (1–240 months), and median duration of renal disease was 20.6 months (0.6–204 months). Fast plasma glucose was 7.60 ± 3.13 mmol/L and postprandial plasma glucose was 13.23 ± 4.67 mmol/L. HbA1c concentration was 7.8 ± 2.0%. Urine protein excretion was 3.6 ± 3.0 g/24 h.
The differential diagnostic model was based on the logistic regression model: \( \pi = e^{z(1 + \gamma)} \), where \( \pi \) is the probability, \( e \) is mathematical constant and \( z = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \ldots + \beta_n x_n \), where \( \beta \) is estimator. In our differential diagnostic model, \( \pi \) is the probability of DN diagnosis (\( P_{\text{DN}} \)), \( x \) represents the five predictors, \( \alpha \) is the constant and \( \beta \) is the coefficient estimator; then \( z = -13.5922 + 0.0371 Dm + 0.0395 Bp + 0.3224 Gh - 4.4552 Hu + 2.9613 Dr \). The standard error, \( P \) value and odds ratio (OR) are shown in Table 4.

**Table 1.** Variety of non-diabetic renal diseases

<table>
<thead>
<tr>
<th>Pathological types</th>
<th>Case</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA nephropathy</td>
<td>17</td>
<td>34.0</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
<td>11</td>
<td>22.0</td>
</tr>
<tr>
<td>Mesangial proliferative GN( ^4 )</td>
<td>7</td>
<td>14.0</td>
</tr>
<tr>
<td>HBV-associated GN</td>
<td>4</td>
<td>8.0</td>
</tr>
<tr>
<td>Minor glomerular abnormalities</td>
<td>3</td>
<td>6.0</td>
</tr>
<tr>
<td>Minimal change disease</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Hypertensive nephrosclerosis</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>FSFS</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Crescentic GN</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Lupus glomerulonephritis</td>
<td>1</td>
<td>2.0</td>
</tr>
</tbody>
</table>

**Table 2.** Clinical features and comorbidities

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>DN (n = 60)</th>
<th>NDRD (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematuria</td>
<td>10 (16.7%)</td>
<td>34 (68.0%)( ^1 )</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>25 (41.7%)</td>
<td>13 (26.0%)( ^1 )</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>21 (35.0%)</td>
<td>5 (10.0%)( ^1 )</td>
</tr>
<tr>
<td>Hypertension</td>
<td>46 (76.7%)</td>
<td>25 (50.0%)( ^1 )</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>39 (65.0%)</td>
<td>38 (76.0%)( ^1 )</td>
</tr>
<tr>
<td>Hyperuricaemia</td>
<td>13 (21.7%)</td>
<td>14 (28.0%)( ^1 )</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>32 (53.3%)</td>
<td>17 (34.0%)( ^1 )</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>46 (76.7%)</td>
<td>5 (10.0%)( ^1 )</td>
</tr>
</tbody>
</table>

\( ^1 P < 0.05, ^2 P < 0.01 \text{ versus DN.} \)

**Pathological types**

In the present study, 110 patients were finally included, of which 60 cases were diagnosed as DN while 50 were NDRD. Our results showed that the NDRD group consisted of many pathological types. IgA nephropathy was most common, accounting for 34% of all NDRD. Membranous nephropathy ranked second accounting for 22%, followed by mesangial proliferative glomerulonephritis (14%), not including IgA nephropathy and other types (Table 1).

**Clinical manifestations**

Table 2 shows that most patients were haematuric in the NDRD group, which accounted for 68%, while the proportion in the DN group was relatively low (16.7%). Contrarily, severe proteinuria was common in the DN group. Nearly half of the patients had proteinuria of nephrotic range. The prevalence of hypertension and renal insufficiency was also significantly higher in the DN group. Also, diabetic retinopathy was predominant in DN (76.7%). Some other indices were different between two groups as well, which are listed in Table 3.

**Correlating factors**

Univariate regression analysis indicated that many indices such as diabetes duration, systolic Bp, HbA1c concentration, serum creatinine, proteinuria, haematuria, urine osmotic pressure and kidney volume were correlated with diagnosis of DN. Concomitant cardiovascular disease and diabetic retinopathy were also the correlating factors. By stepwise forward multivariate regression analysis, we identified diabetes duration, systolic Bp, HbA1c, haematuria and retinopathy as independent correlating factors. Their estimators were 0.0371, 0.0395, 0.3224, –4.4552 and 2.9613, respectively; the constant was –13.5922. The standard error, P value and odds ratio (OR) are shown in Table 4.

**Development of the differential diagnostic model**

The differential diagnostic model was based on the logistic regression model: \( \pi = e^{z(1 + \gamma)} \), where \( \pi \) is probability, \( e \) is mathematical constant and \( z = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \ldots + \beta_n x_n \), where \( \beta \) is estimator. In our differential diagnostic model, \( \pi \) is the probability of DN diagnosis (\( P_{\text{DN}} \)), \( x \) represents the five predictors, \( \alpha \) is the constant and \( \beta \) is the coefficient estimator; then \( z = -13.5922 + 0.0371 Dm + 0.0395 Bp + 0.3224 Gh - 4.4552 Hu + 2.9613 Dr \). The standard error, P value and odds ratio (OR) are shown in Table 4.
A differential diagnostic model of renal diseases in diabetes

Table 4. Multivariate regression analysis results

<table>
<thead>
<tr>
<th>Indicators</th>
<th>β-estimate</th>
<th>Standard error</th>
<th>P-value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes duration (month)</td>
<td>0.0371</td>
<td>0.0126</td>
<td>0.006</td>
<td>1.038</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>0.0395</td>
<td>0.0139</td>
<td>0.048</td>
<td>1.040</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>0.3224</td>
<td>0.1108</td>
<td>0.038</td>
<td>1.385</td>
</tr>
<tr>
<td>Haematuria (yes/no)</td>
<td>-4.4552</td>
<td>1.0305</td>
<td>&lt;0.001</td>
<td>0.029</td>
</tr>
<tr>
<td>Diabetic retinopathy (yes/no)</td>
<td>2.9613</td>
<td>0.9637</td>
<td>0.002</td>
<td>18.326</td>
</tr>
</tbody>
</table>

Table 5. Predictive value

<table>
<thead>
<tr>
<th>Back-substitution test</th>
<th>Validation cohort test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DN</td>
</tr>
<tr>
<td>Diagnosed as DN</td>
<td>54</td>
</tr>
<tr>
<td>Diagnosed as NDRD</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>90.0%</td>
</tr>
<tr>
<td>Specificity</td>
<td>92.0%</td>
</tr>
<tr>
<td>Positive predictive</td>
<td>93.1%</td>
</tr>
<tr>
<td>Negative predictive</td>
<td>88.5%</td>
</tr>
<tr>
<td>Total consistency</td>
<td>90.9%</td>
</tr>
</tbody>
</table>

\[
[1 + \exp(-13.5922 + 0.0371 \times 180 + 0.0395 \\
\times 160 + 0.3224 \times 7 - 4.4552 \times 0 + 2.9613 \times 1)]
\]
\[
= 101.89063/102.89063
\]
\[
= 0.99028094
\]

(b) A typical NDRD: Only 5 years of diabetes, systolic Bp is 130 mmHg, HbA1c is 6%, with haematuria but no retinopathy. The diagnosis should be NDRD due to the small value of the calculated probability (<0.001):

\[
P_{DN} = \exp(-13.5922 + 0.0371Dm + 0.0395Bp + 0.3224Gh - 4.4552Hu + 2.9613Dr)/
\]
\[
[1 + \exp(-13.5922 + 0.0371Dm + 0.0395Bp + 0.3224Gh - 4.4552Hu + 2.9613Dr)]
\]
\[
= \exp(-13.5992 + 0.0371 \times 60 + 0.0395 \times 130 \\
+ 0.3224 \times 6 - 4.4552 \times 1 + 2.9613 \times 0)/
\]
\[
[1 + \exp(-13.5992 + 0.0371 \times 60 + 0.0395 \\
\times 130 + 0.3224 \times 6 - 4.4552 \times 1 + 2.9613 \times 0)]
\]
\[
= 0.00015814/1.0001581
\]
\[
= 0.00015812
\]

Sensitivity and specificity of the differential diagnostic model

The back-substitution test showed that this model had a sensitivity of 90.0%, a specificity of 92.0%, a positive predictive value of 93.1%, a negative predictive value of 88.5% and a total consistency rate of 90.9%. Furthermore, we used this model to predict the diagnosis of later biopsy type 2 diabetic patients. During the following 2 years after model establishment (January 2005–December 2006), 21 patients were screened out for biopsy based on the same inclusion criteria. In this validation cohort, 8 were predicted as DN and 13 as NDRD by this diagnostic model. Then, by kidney biopsy, 10 patients were proved to be DN, 11 NDRD; the total consistency rate was 90.5%. The predictive value of this model seemed to be good (Table 5). In the ROC curve we made (Figure 1), the area under the curve was 0.968. By comparison with other diagnostic methods, this diagnostic model including five variables showed an advantage in clinical prediction (Table 6).
Discussion

The prevalence of NDRD in the diabetic patients who underwent kidney biopsy varies from 10% to 85% in different reports [8–11]. Our study showed that 45.5% of biopsied type 2 diabetic patients were diagnosed as NDRD. IgA nephropathy was the most common, accounting for 34% of all the NDRD. This indicated that we should pay more attention to the probability of non-diabetic renal injuries, especially IgA nephropathy in diabetic patients. Moreover, together with non-IgA mesangial proliferative glomerulonephritis (14%), all 48% of NDRD were predominantly mesangial proliferative glomerulonephritis. The number was similar to those in other Asian reports.

Diabetes duration is an indicator of DN in type 2 DM. Patients with persistent proteinuria and a relatively short period of diabetes should be examined carefully to identify NDRD. In DN, it often takes quite a long period of time to go from micro-albuminuria to macro-albuminuria, and even renal failure. DN is one of the chronic complications of diabetes. Clinical abnormalities are often detected 5–10 years after onset or diagnosis of DM. The patient with a relatively shorter diabetes duration is probably thought to be NDRD.

We found that the mean systolic blood pressure of the DN group was higher than that of the NDRD group (149.2 ± 22.3 versus 133.7 ± 17.9 mmHg, \( P < 0.01 \)). Hypertension could occur in many advanced renal diseases, but it is more prevalent in diabetic patients. The reason is more complex, as some mechanisms may aggravate hypertension, such as water–sodium retention, RAS activity, sympathetic overactivity and endothelial cell dysfunction. Even the hereditary relationship between hypertension and DN may play a role [12]. Therefore, the DN group manifested hypertension more often and more severely than the NDRD group in our study.

In the present study, the prevalence of haematuria was quite different between the two groups (17% versus 68%). Severe proteinuria is common in DN, but haematuria is rarely found. Meanwhile, many entities of NDRD, such as IgA nephropathy, often manifest microscopic or gross haematuria. Thus, haematuria becomes an important differential indicator, which is supported by the study of Mak et al. [13].

Diabetic retinopathy (DR) is one of the microvascular complications of DM, which might have the same pathogenetic pathways as DN. Retinopathy, when it coexists with nephropathy (usually called renal-retinal syndrome), is thought to be a window of renal complication. Diabetic retinopathy may serve as an indicator of DN. The relationship between retinopathy and nephropathy in type 1 DM has been demonstrated in some studies [14,15]. In type 2 DM, it was confirmed by Fioretto’s cohort [16] that almost all microalbuminuric patients had DR and all patients with proliferative DR had typical DN. Results of Parving et al. [17] showed that all the proteinuric NIDDM patients with DR had DN. On the other hand, Parving believed that lack of DR was a poor predictor of NDRD since the chance for DN or NDRD was fifty-fifty. In our study, 90% of type 2 DM patients with diabetic retinopathy were DN and 76% of diabetic patients without retinopathy were NDRD. It seemed that non-DR was a rather of good indicator for NDRD.

Though many indicators have been found to be important distinguishing DN from NDRD in the literature, it is still unknown how to identify DN effectively, safely and scientifically. Kidney biopsy is the most effective method to identify DN in type 2 DM, but it can not be performed on all the patients due to factors such as anticoagulation, active bleeding, unilateral nephrectomy or reluctant to biopsy. Basically, people used to believe that a biopsy had to be taken to clinically diagnose DN. The diagnosis criteria were developed as follows: persistent albuminuria, presence of diabetic retinopathy and absence of any clinical or laboratory evidence of other kidney or renal tract disease [17]. Also, Glassock [18] had presented biopsy criteria previously, but Serra [19] thought these biopsy criteria were not useful in identifying patients with other renal diseases. Based on this, some researchers investigated the frequencies of NDRD in diabetic patients, and the results varied. The inclusion criteria may play a role and derive conflicting conclusions.

In the present study, patients were divided into two groups according to pathological changes. For the purpose of better discrimination, we omitted the overlapping group (1.8%, two cases, one with HBV-associated GN, one with IgA nephropathy) and one ambiguous case (0.9%, a case who showed slight mesangial proliferation in LM, no immune deposits in IF, but without EM results). Because of the small proportion of omitted patients, the predictive value was scarcely influenced.

We found that DN and NDRD had different manifestations. Some important characteristics related to clinical differentiation may serve as indicators. Through logistic regression analysis, we identified diabetes duration, systolic blood pressure, concentration of HbA1c, haematuria and diabetic retinopathy as five major differential indicators. Though they had been mentioned in previous literature, we arranged the five indicators in an equation and developed a differential diagnostic model, which could give a quantified probability of DN. The back-substitution test indicated that this differential diagnostic model had perfect sensitivity (90%) and specificity (92%), giving a clear distinction between DN and NDRD. Figure 1 shows that the AUC (0.968) was very close to 1.0 which indicated a perfect predictive power. The following prospective test

<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Youden's index</th>
<th>Total consistency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic equation</td>
<td>90.0%</td>
<td>92.0%</td>
<td>82.0%</td>
<td>90.9%</td>
</tr>
<tr>
<td>Retinopathy (±)</td>
<td>76.7%</td>
<td>90.0%</td>
<td>66.7%</td>
<td>82.7%</td>
</tr>
<tr>
<td>Haematuria (±)</td>
<td>83.3%</td>
<td>68.0%</td>
<td>51.3%</td>
<td>76.4%</td>
</tr>
</tbody>
</table>

Table 6. Comparison of three diagnostic methods
on the validation cohort showed that the sensitivity was 80% and the specificity was 100%. The predictive value of this model seemed to be good.

We compared different diagnostic methods (by the diagnostic model we had developed or by a simpler algorithm of one important variable, such as retinopathy or haematuria). Retinopathy, although believed to be an important predictor, could not do as well as the equation including five variables. Similarly, considering haematuria alone resulted in lower predictive value. We suppose that each variable represents only a part of the information; the more information retained, the more accurate the equation will be. The comparison results verified the advantage of our diagnostic model.

This discriminant model was based on logistic regression, which is an important method of discriminant analysis and was also applied to diagnosis of some other diseases in recent literature [20,21]. In this study, we constructed a differential diagnostic model composed of five clinical indices, which could give a quantified probability of DN. It may be useful to physicians’ daily work. It should be noted that this is a monocentric study, and the patients were selected only from the nephrology clinic of PLA General Hospital. Therefore, this diagnostic model should be restricted to the daily work of nephrologists in hospitals of the similar level. Moreover, the components of NDRD vary enormously across the world, so it is better to apply this model only in the same ethnic region as the study. Despite the above limitations, this model has provided a quantitative method for clinical differentiation and might help medical researchers to develop a more rational and effective kidney biopsy criteria in type 2 diabetic patients.

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Conflict of interest statement. None declared.

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