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Construction of a Risk Prediction Model for Diabetic Nephropathy Based on the Urinary Microalbumin-to-Creatinine Ratio and Blood Markers

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Abstract

Objective: To investigate the predictive value of blood creatinine (Cr), blood urea (Ur), blood uric acid (Ua), serum homocysteine (Hcy), glycated hemoglobin (HbA1c), and the urinary microalbumin (MAlb)-to-urinary creatinine (uCr) ratio in the diagnosis of diabetic nephropathy (DN). **Methods:** A retrospective study design was employed. A total of 105 patients diagnosed with diabetic nephropathy (DN) at the Third People's Hospital of Nanning from January 2023 to December 2025 were enrolled as study group A, and 118 patients with simple diabetes mellitus (DM) were enrolled as study group B. General data and levels of various detection indicators were compared between the two groups. Multivariate logistic regression was used to analyze the influencing factors for the occurrence of diabetic nephropathy in diabetic patients. Receiver operating characteristic (ROC) curves were plotted to analyze the predictive value of single and combined detection of Ur, Ua, Hcy, HbA1c, and MAlb/uCr for diabetic nephropathy. **Results:** The levels of Cr, Ur, Ua, Hcy, HbA1c, and MAlb/uCr in the diabetic nephropathy group were significantly higher than those in the simple diabetes group, with statistically significant differences ($P < 0.05$). Multivariate logistic regression analysis showed that elevated levels of Cr (OR = 1.028, 95% CI: 1.006 - 1.050) and MAlb/uCr (OR = 1.006, 95% CI: 1.003 - 1.009) were independent risk factors for the development of DN in DM patients ($P < 0.05$). ROC curve analysis showed that the area under the curve (AUC) for the combined detection of Ur, Ua, Hcy, HbA1c, and MAlb/uCr in predicting the development of DN in DM patients was

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0.863, with a sensitivity of 77.10% and a specificity of 87.30%, which were superior to single detection of each indicator. **Conclusion:** Elevated levels of Cr and MAlb/uCr are independent risk factors for the development of diabetic nephropathy in diabetic patients. Combined detection of Ur, Ua, Hcy, HbA1c, and MAlb/uCr can significantly improve the diagnostic efficiency for diabetic nephropathy, providing an important laboratory basis for early clinical screening and intervention of diabetic nephropathy.

Keywords

Urinary Microalbumin-to-Creatinine Ratio, Diabetic Nephropathy, Blood Creatinine, Homocysteine, Glycated Hemoglobin, Predictive Value

1. Introduction

Diabetic Nephropathy (DN) is one of the most common and severe microvascular complications of diabetes mellitus and is the leading cause of end-stage renal disease (ESRD) worldwide [1]-[3]. Clinical data indicate that the incidence of DN among diabetic patients ranges from 20% to 40%, and approximately 40% of patients with ESRD require hemodialysis or kidney transplantation, imposing a substantial medical burden on families and society. Therefore, early diagnosis and intervention of DN are crucial for improving patient prognosis [3].

Currently, commonly used clinical renal function indicators such as creatinine, urea, and uric acid lack sufficient accuracy in the early diagnosis of DN, making it difficult to detect abnormalities before organic damage occurs in the renal tissue. The 24-hour urinary protein excretion rate is a classic method for assessing renal function abnormalities, but this test suffers from issues such as time-consuming sample collection, subjective procedures, and susceptibility of results to storage conditions, hindering its routine clinical application [4]. Serum homocysteine (Hcy) is a sensitive indicator for assessing kidney injury, capable of early reflection of the degree of renal microvascular damage. Glycated hemoglobin (HbA1c) stably reflects the patient's blood glucose control level over the preceding 2 - 3 months and is closely related to the occurrence and development of DN [5]. The urinary microalbumin-to-creatinine ratio (MAlb/uCr) is an important marker for early kidney damage, capable of detecting abnormalities before significant structural damage occurs in the nephron, and holds high diagnostic value for chronic kidney disease. However, its sensitivity and specificity when used alone still have limitations [6].

Based on this, this study retrospectively analyzes the clinical testing data of patients with diabetic nephropathy and those with simple diabetes mellitus to investigate the predictive value of MAlb/uCr combined with blood indicators such as Cr, Ur, Ua, Hcy, and HbA1c in the diagnosis of DN. The aim is to identify a more efficient and convenient combination of indicators for early DN screening in clinical practice and provide a reference basis for early intervention in DN.

2. Materials and Methods

2.1. General Information

This study is a retrospective analysis. The research subjects were diabetes-related patients treated at the Third People's Hospital of Nanning from January 2023 to December 2025. They were divided into two groups based on the presence or absence of diabetic nephropathy: Study group A (DN group) consisted of 105 patients with diabetic nephropathy; Study group B (DM group) consisted of 118 patients with simple diabetes mellitus, showing no renal function abnormalities or kidney damage. A total of 286 diabetic patients were initially screened, of which 38 were excluded due to incomplete data, 15 due to other kidney diseases, and 10 due to malignant tumors or severe cardiovascular/cerebrovascular diseases, resulting in 223 eligible cases.

Inclusion Criteria: 1) DM diagnosis met the diagnostic criteria in the 2020 edition of the "Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (Part 1)" [7]; 2) DN diagnosis met the relevant criteria in the "Clinical Guidelines for the Prevention and Treatment of Diabetic Kidney Disease in China" [8], *i.e.*, persistent microalbuminuria or more severe proteinuria occurring on the basis of DM, or a decrease in glomerular filtration rate (<60 ml/min/1.73 m^2), after excluding other kidney diseases; 3) Normal liver function, no recent use of drugs affecting renal function; 4) Complete clinical data, with simultaneous completion of Cr, Ur, Ua, Hcy, HbA1c, and MAlb/uCr tests. For the simple DM group, in addition to meeting the DM diagnostic criteria, patients were required to have a urinary albumin excretion rate (UAER) < 30 mg/24h or a urinary albumin-to-creatinine ratio (UACR) < 30 mg/g, and an estimated glomerular filtration rate (eGFR) ≥ 60 ml/(min·1.73m^2), to exclude early kidney injury.

Exclusion Criteria: 1) Patients with concurrent malignant tumors; 2) Patients with clear kidney disease caused by other reasons; 3) Patients with severe organic diseases of the heart, lung, brain, etc.; 4) Patients with infectious diseases or autoimmune diseases; 5) Patients with incomplete clinical data.

This study protocol was reviewed and approved by the Medical Ethics Committee of the Third People's Hospital of Nanning. The collection of clinical data for all research subjects complied with relevant medical ethics requirements.

2.2. Research Methods

Gender, age, and results of various laboratory tests for all enrolled patients were retrospectively collected through the hospital information system. Fasting peripheral venous blood and fresh morning urine samples were collected from all patients in the early morning. Testing for blood creatinine (Cr), blood urea (Ur), blood uric acid (Ua), serum homocysteine (Hcy), glycated hemoglobin (HbA1c), urinary microalbumin (MAlb), and urinary creatinine (uCr) was performed using a Beckman Coulter 5800 or Hitachi 7180 automatic biochemical analyzer. All test-

ing operations strictly followed the instructions of the instruments and reagent kits to ensure the accuracy of the test results.

2.3. Observation Indicators

1) Comparison of general data gender, age and levels of Cr, Ur, Ua, Hcy, HbA1c, and MAlb/uCr between patients in study group A and study group B; 2) Use of multivariate logistic regression analysis to identify independent risk factors for the development of diabetic nephropathy in diabetic patients; 3) Use of receiver operating characteristic (ROC) curves to analyze the diagnostic efficacy of single and combined detection of Ur, Ua, Hcy, HbA1c, and MAlb/uCr for diabetic nephropathy, calculating the area under the curve (AUC), sensitivity, specificity, and optimal cut-off values for each indicator. The combined prediction model was constructed using multivariate logistic regression analysis, with the occurrence of DN as the dependent variable and Ur, Ua, Hcy, HbA1c, and MAlb/uCr as independent variables to calculate the combined predicted probability, which was then used to plot the ROC curve for combined detection.

2.4. Statistical Methods

SPSS 29.0 statistical software was used for data processing and analysis. Measurement data were first tested for normality. Data following a normal distribution were expressed as mean ± standard deviation ($\overline{x} \pm s$), and comparisons between two groups were performed using the t-test. Measurement data with a skewed distribution were expressed as median (M) and interquartile range (P25; P75), and comparisons between two groups were performed using the Mann-Whitney U rank-sum test. Count data were expressed as number of cases and percentage (n, %), and comparisons between groups were performed using the χ^2 test. Multivariate logistic regression analysis was used to identify independent risk factors for the occurrence of diabetic nephropathy, with the occurrence of DN as the dependent variable (yes = 1, no = 0) and indicators with statistically significant differences as independent variables. with adjustment for age and sex, ROC curves were plotted to analyze the diagnostic efficacy of each indicator, calculating AUC, 95% confidence interval (CI), sensitivity, specificity, and optimal cut-off value. A P-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of General Data and Test Indicator Levels between the Two Groups

There was no statistically significant difference in age between the two groups (P > 0.05), the difference in gender composition between the two groups was statistically significant (P < 0.05). The levels of Cr, Ur, Ua, Hcy, HbA1c, and MAlb/uCr in study group A were significantly higher than those in study group B, with highly statistically significant differences in all indicators between the groups (P < 0.001). See Table 1.

Table 1. Comparison of general data between the two groups.

Indicator	Group A (n = 105)	Group B (n = 118)	Statistic	P value
Gender (n, %)	Male 73 (69.52); Female 32 (30.48)	Male 66 (55.93); Female 52 (44.07)	$\chi^2 = 4.371$	0.037
Age	**58.4 ± 10.2**	**56.9 ± 9.8**	**1.124**	**0.262**
Cr [M (P25, P75), μmol/L]	81.00 (56.50, 128.00)	67.00 (56.00, 81.00)	z = −783	<0.001
Ur [M (P25, P75), mmol/L]	7.30 (5.26, 10.18)	5.39 (4.53, 6.18)	z = −0.531	<0.001
Ua [M (P25, P75), μmol/L]	375.00 (313.00, 450.50)	317.50 (275.75, 374.00)	z = −0.961	<0.001
Hcy [M (P25, P75), μmol/L]	12.98 (9.81, 16.76)	10.17 (8.65, 12.03)	z = −0.646	<0.001
HbA1c [M (P25, P75), %]	8.76 (7.08, 11.70)	7.25 (6.31, 10.35)	z = −282	0.001
MAlb/uCr [M (P25, P75), mg/g]	185.00 (59.00, 949.50)	19.50 (11.00, 49.50)	z = −9.114	<0.001

3.2. Multivariate Logistic Regression Analysis of Diabetic Nephropathy Occurrence

Using the occurrence of DN in diabetic patients as the dependent variable, and Cr, Ur, Ua, Hcy, HbA1c, and MAlb/uCr as independent variables, with adjustment for age and sex, multivariate logistic regression analysis was performed. The results showed that elevated levels of Cr and MAlb/uCr were independent risk factors for the occurrence of DN in diabetic patients ($P < 0.05$), while Ur, Ua, Hcy, and HbA1c were not independent risk factors for DN occurrence ($P > 0.05$). See Table 2.

Table 2. Multivariate logistic regression analysis.

Factor	β value	S $\bar{x}$ value	Wald χ^2 value	OR value (95% CI)	P value
Gender	**0.452**	**0.321**	**1.983**	**1.571**	**0.159**
Age	**0.023**	**0.015**	**2.351**	**1.023**	**0.125**
Cr	0.027	0.011	6.156	1.028 (1.006 - 1.050)	0.013
Ur	0.095	0.059	2.615	1.100 (0.980 - 1.234)	0.106
Ua	0.002	0.002	1.149	1.002 (0.998 - 1.006)	0.284
Hcy	0.020	0.050	0.163	1.020 (0.926 - 1.125)	0.687
HbA1c	0.126	0.065	3.698	1.134 (0.998 - 1.289)	0.054
MAlb/uCr	0.006	0.002	14.010	1.006 (1.003 - 1.009)	<0.001

3.3. Predictive Value of Single and Combined Detection of Indicators for Diabetic Nephropathy

ROC curve analysis results showed that among single indicator detections, MAlb/uCr had the highest AUC (0.854), followed by Ur (0.715), Hcy (0.680), Ua (0.654), and HbA1c (0.627). The combined detection of Ur, Ua, Hcy, HbA1c, and MAlb/uCr yielded an AUC of 0.863 (95% CI: 0.814 - 0.913), with a sensitivity of 77.10% and a specificity of 87.30%, demonstrating superior diagnostic efficacy compared to single detection of each indicator. The combined ROC curve in this study was

plotted based on the combined predicted probability calculated from a multivariate logistic regression model, which did not include Cr. The main reason is that Cr is more commonly used in clinical practice to assess established renal impairment, whereas the combination of Ur, Ua, Hcy, HbA1c, and MAlb/uCr focuses more on integrating metabolic and early injury markers. The good performance of this combination without Cr suggests its clinical utility. See Figure 1 and Table 3.

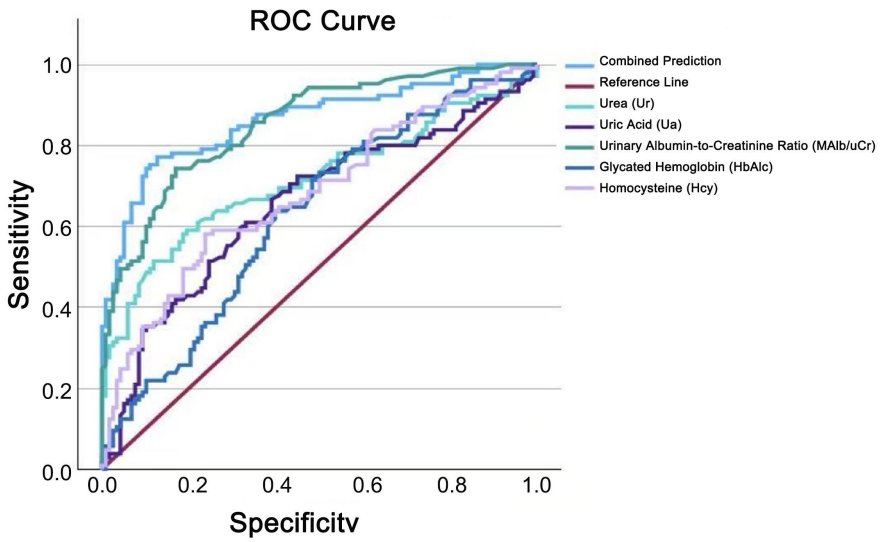

Figure 1. ROC curve.

Table 3. ROC curve parameters for single and combined detection of indicators in predicting diabetic nephropathy.

Indicator	AUC	95% CI	Sensitivity (%)	Specificity (%)	Cut-off value
Ur	0.715	0.953 - 0.998	59.00	80.50	6.455 mmol/L
Ua	0.654	0.580 - 0.727	61.00	66.90	355.500 μmol/L
Hcy	0.680	0.610 - 0.751	58.10	76.30	12.095 μmol/L
HbA1c	0.627	0.554 - 0.700	63.80	60.20	7.950%
MAlb/uCr	0.854	0.805 - 0.902	74.30	83.10	64.500 mg/g
Combined	0.863	0.814 - 0.913	77.10	87.30	—

4. Discussion

The occurrence and development of diabetic nephropathy is a complex process involving multiple factors. A prolonged hyperglycemic state can damage the glomerular filtration membrane and impair renal microvascular circulation, ultimately leading to irreversible structural and functional damage to the nephron [9]. Due to the lack of typical clinical symptoms in the early stage of DN, most patients are already in the middle or late stages upon diagnosis, missing the optimal window for intervention. Therefore, searching for sensitive and specific early

diagnostic markers is a key focus of clinical research.

The results of this study show that the levels of Cr, Ur, Ua, Hcy, HbA1c, and MAlb/uCr in the DN group were significantly higher than those in the simple DM group, suggesting that these indicators are closely related to the occurrence and development of DN. Among them, the difference in MAlb/uCr between the two groups was the most significant. This is because the glomerular filtration membrane in healthy individuals possesses an intact barrier function, resulting in very low urinary excretion of microalbumin. However, long-term hyperglycemia in diabetic patients can damage the charge and size selectivity barriers of the glomerular filtration membrane, leading to abnormal urinary albumin excretion. Furthermore, urinary creatinine corrects the urinary microalbumin test results, eliminating the effects of urine concentration or dilution, making the test results more stable and sensitive in reflecting the degree of renal function impairment [10]. Multivariate logistic regression analysis further confirmed that MAlb/uCr is an independent risk factor for DN occurrence, consistent with the findings of Wu Dongna *et al.* [11], suggesting that MAlb/uCr can serve as a core indicator for assessing renal function impairment in diabetic patients.

Blood creatinine is a classic indicator reflecting glomerular filtration function. This study found that an elevated Cr level is another independent risk factor for DN occurrence, with an OR value of 1.028, indicating that for every 1 unit increase in Cr level, the risk of developing DN in diabetic patients increases by 2.8%. The study by Lin Huijin *et al.* [12] also pointed out that Cr has good value for the early diagnosis of DN, which is consistent with the results of this study. However, the study by Hou Qian *et al.* [13] suggested that Cr alone has poor sensitivity for DN and cannot truly reflect the severity of DN, which also indicates the limitations of single-indicator testing and the need for combination with other indicators.

HbA1c stably reflects the long-term blood glucose control level in diabetic patients. In this study, the HbA1c level in the DN group was significantly higher than that in the DM group. ROC curve analysis showed its optimal cut-off value was 7.950%, which is generally consistent with the study by Mu Weidong *et al.* [14] suggesting that controlling HbA1c below 7.0% can delay the progression of DN, indicating that poor long-term glycemic control is an important contributor to DN occurrence. Serum Hcy level is closely related to renal microvascular damage. The study by Guan Haifei *et al.* [15] found that high expression of serum Hcy damages endothelial cells and glomerular function, exacerbating renal microcirculatory disturbances. The significantly elevated Hcy level in the DN group in this study also validates this conclusion. Furthermore, the significantly elevated levels of Ur and Ua in the DN group suggest that the renal excretory function has already become abnormal, accompanying the progression of renal function impairment.

The ROC curve analysis results of this study show that the diagnostic efficacy of single indicator detection is limited. Among them, MAlb/uCr had the highest diagnostic efficacy, but its AUC was only 0.854. However, when Ur, Ua, Hcy, and HbA1c were combined with MAlb/uCr for detection, the AUC increased to 0.863,

and the sensitivity and specificity reached 77.10% and 87.30%, respectively, significantly improving the diagnostic efficacy. This result suggests that a single indicator is difficult to fully capture the occurrence and development process of DN. In contrast, combined detection integrates information from multiple aspects such as renal function, blood glucose control, and inflammatory damage, reflecting the state of renal impairment in diabetic patients from different angles, thereby improving the accuracy of early DN diagnosis. In recent years, several studies have also confirmed the value of multi-indicator combined models in early DN screening. For example, Wang Zuolong *et al.* [16] found that combined detection of blood and urine indicators could increase the AUC for early DN diagnosis to above 0.87, which is similar to the findings of this study.

This study provides a new combination of indicators for early clinical screening of DN. The combined detection of Ur, Ua, Hcy, HbA1c, and MAlb/uCr is convenient to operate and yields stable results. It does not require additional sample collection and is suitable for routine clinical practice, particularly holding significant application value for early DN screening in primary healthcare institutions.

5. Conclusion

Elevated levels of blood creatinine and the urinary microalbumin-to-creatinine ratio are independent risk factors for the development of diabetic nephropathy in diabetic patients. Combined detection of blood urea, blood uric acid, serum homocysteine, glycated hemoglobin, and the urinary microalbumin-to-creatinine ratio can significantly improve the diagnostic efficacy for diabetic nephropathy. This combination possesses high clinical predictive value, can provide important laboratory evidence for the early screening and intervention of diabetic nephropathy, and is worthy of clinical promotion and application.

6. Limitations of the Study

This study is a single-center retrospective study with a limited sample size, which may affect the generalizability of the findings. Future multi-center, large-sample prospective studies are needed to further validate the conclusions. Additionally, since MAlb/uCr and renal function indicators are themselves important references for the diagnosis of DN, their simultaneous use as predictors may introduce a degree of incorporation bias. This study could not completely avoid the impact of this bias on the assessment of diagnostic efficacy in its methodology, and further validation in prospective studies is needed. This study did not include novel kidney injury markers such as cystatin C or neutrophil gelatinase-associated lipocalin (NGAL) to further optimize the indicator combination. Subsequent studies could incorporate more novel markers to explore more efficient early diagnostic models for DN.

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Conflicts of Interest

All authors of this study declare that during the research process and manuscript preparation, there were no personal or commercial conflicts of interest. The research data are authentic and objective, without fabrication or manipulation. All authors have reviewed and approved the submission of this manuscript.

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