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Predictive value of the prognostic nutritional index for rapid kidney function decline in patients with type 2 diabetes mellitus

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Abstract: Objective To investigate the role of the prognostic nutritional index (PNI) in predicting renal function changes in patients with type 2 diabetes mellitus (T2DM). **Methods** A retrospective study was conducted with 366 T2DM patients who visited the First People's Hospital of Wuhu from January 2015 to January 2021. Follow-up was performed after treatment, with the final follow-up in August 2024. Clinical data were collected, and the annual decline in the estimated glomerular filtration rate (eGFR) was calculated. Patients were divided into two groups: the rapid kidney function decline (RKFD) group (n=109) and the non-RKFD group (n=257), with RKFD defined as an annual eGFR decline over 3 mL/ (min·1.73 m^2). Spearman correlation analysis was used to explore the relationship between PNI and various indicators in T2DM patients. Multivariate logistic regression analysis was performed to identify the factors influencing RKFD in T2DM patients. The predictive value of PNI was evaluated using receiver operating characteristic (ROC) curves. **Results** The median follow-up period for the 366 T2DM patients was 5 years, with 109 (29.78%) patients experiencing RKFD. The baseline level of glycated hemoglobin (HbA_{1C}) in the RKFD group was higher than that in the non -RKFD group [9.40% (7.33%, 10.85%) *vs* 8.20% (6.70%, 9.95%), Z=3.240, P=0.001]. Compared with non-RKFD group, the albumin, eGFR, lymphocyte count, red blood cell count, platelet count, hemoglobin, and PNI were lower in the RKFD group (P<0.05). Spearman correlation analysis showed that PNI in T2DM patients was positively correlated with uric acid, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, albumin, fasting C-peptide, white blood cell count, lymphocyte count, red blood cell count, platelet count, hemoglobin, and eGFR, respectively (P<0.05), and was negatively correlated with HbA1C (r=-0.163, P=0.002). Multivariate logistic regression analysis indicated that independent factors influencing RKFD included PNI (OR=0.846, 95% CI: 0.798- 0.898, P<0.01) and HbA_{1C} (OR=1.121, 95% CI: 1.009- 1.247, P=0.034). ROC curve analysis showed that the area under the curve for PNI in predicting RKFD in T2DM patients was 0.752, with an optimal cut-off value of 49.33, sensitivity of 0.658, and specificity of 0.789. **Conclusion** T2DM patients with lower PNI are at higher risk of RKFD, and PNI can be served as an important indicator for assessing the renal function prognosis in T2DM patients.

Keywords: Prognostic nutritional index; Type 2 diabetes mellitus; Rapid kidney function decline; Diabetic kidney disease; Glomerular filtration rate; Glycated hemoglobin Fund program: Key Scientific Research Project of Natural Science of Universities in Anhui Province (2022AH050752); Natural Science Research Project of Universities in Anhui Province (KJ2020A0341)

Type 2 diabetes mellitus (T2DM) is the common chronic metabolic diseases worldwide, with its incidence and prevalence increasing year by year [1-2]. Epidemiological studies have shown that approximately 40% of diabetic patients eventually progress to diabetic kidney disease (DKD) [3]. DKD is the primary cause of end-stage renal disease, severely affecting patients' quality of life and prognosis [4]. The early stage of DKD development typically presents no significant symptoms, manifesting only as mild proteinuria. Moreover, the lack of effective biomarkers for accurate prediction of early renal function decline makes early diagnosis difficult [5-6]. Although interventions such as glycemic control, blood pressure management, and renin-angiotensin system inhibition can slow the progression of DKD, a considerable proportion of T2DM patients still experience rapid kidney function decline (RKFD) [7]. In recent years, attention has been paid to the impact of lifestyle factors and nutritional status on T2DM. The prognostic nutritional index (PNI), as an important indicator for evaluating patients' nutritional status, has been widely used to assess the prognosis of various diseases such as tumors, cardiovascular diseases, and chronic kidney diseases [8-9]. Low PNI levels often indicate malnutrition and impaired immune function [10]. PNI has been confirmed to have important clinical predictive value in adverse cardiovascular events related to complications in T2DM patients [11]. However, there are few studies on the predictive value of PNI for RKFD in T2DM patients. This study aims to investigate the predictive value of PNI levels for RKFD in T2DM patients, in order to analyze the role of PNI in predicting changes in renal function in T2DM patients.

1 Materials and methods

1.1 General information

A total of 366 patients with T2DM who visited Wuhu First People's Hospital from January 2015 to January 2021 were retrospectively selected as study subjects. This study

was approved by the Medical Ethics Committee of Wuhu First People's Hospital (approval No.: YYLL20230046).

Inclusion criteria: (1) Meeting the diagnostic criteria for T2DM developed by the WHO in 1999; (2) Age ≥ 18 years; (3) Estimated glomerular filtration rate (eGFR) ≥ 60 mL/(min·1.73 m²) at the first visit; (4) Having at least 1 effective follow-up, which must include fasting serum creatinine test; (5) Complete clinical data.

Exclusion criteria: (1) Complicated with acute kidney injury, kidney diseases caused by other factors, or urinary tract infection; (2) Lactation or pregnancy; (3) Type 1 diabetes mellitus, gestational diabetes mellitus, or other types of diabetes; (4) Severe acute complications such as diabetic ketoacidosis or hyperosmolar coma; (5) Complicated with major diseases such as malignant tumor or severe infection; (6) Complicated with severe organ diseases such as heart or liver diseases.

1.2 Methods

1.2.1 Data collection

(1) Baseline data: gender, age, systolic blood pressure, diastolic blood pressure, etc. (2) Blood markers at the first visit: routine blood test, albumin, blood urea nitrogen, serum creatinine, blood uric acid, fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), glycated hemoglobin (HbA_{1C}), fasting insulin (FINS), fasting C-peptide; eGFR and PNI values were calculated simultaneously. (3) Follow-up data: The follow-up deadline was August 2024. Each outpatient or inpatient visit was regarded as one effective follow-up, with an interval of more than 1 year between two effective follow-ups. The follow-up method was to review medical records in the outpatient or inpatient electronic medical record system. The fasting serum creatinine value from the patient's last outpatient visit or hospitalization was collected, and the eGFR value and annual eGFR decline value were calculated. The formula for PNI calculation [12]: PNI = serum albumin (g/L) + 5 × total peripheral blood lymphocyte count ($\times10^9$/L); eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [13].

1.2.2 Definition of enrollment

Patients were divided into non-RKFD group and RKFD group according to whether renal function declined rapidly. RKFD was defined as an average annual eGFR decline > 3 mL/(min·1.73 m²) [14]. The cut-off value of PNI for predicting RKFD was determined by receiver operating characteristic (ROC) curve analysis.

1.3 Statistical methods

SPSS 27.0 statistical software was used for data analysis. Categorical variables were expressed as cases (%), and comparisons between groups were performed using the χ^2 test. Normally distributed continuous variables were expressed as $\bar{x}\pm s$, and comparisons between groups were performed using the independent sample t-test. Non-normally distributed continuous variables were expressed as M (P_{25}, P_{75}), and differences between the two groups were analyzed using the Mann-Whitney U test. Spearman correlation analysis was used to analyze the correlation between PNI and various indicators. Multivariate logistic regression was used to explore the influencing factors of RKFD in T2DM patients. ROC curves were plotted to calculate the area under the curve (AUC), sensitivity, specificity, and their 95%*CI* of PNI for predicting RKFD. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of baseline data between two groups

A total of 366 T2DM patients were included in this study, with a median follow-up period of 5 years. Among them, 109 patients developed RKFD, with an incidence rate of 29.78% (109/366). Baseline data analysis showed that the level of HbA_{1C} in the RKFD group was higher than that in the non-RKFD group, while albumin, eGFR, lymphocyte count, red blood cell count, platelet count, hemoglobin, and PNI were lower than those in the non-RKFD group (P<0.05). There were no statistically significant differences in gender, age, or other indicators between the two groups (P>0.05). **[Table 1]**

Tab. 1 Comparison of baseline characteristics between non-RKFD group and RKFD group

Item	Non-RKFD group (n=257)	RKFD group (n=109)	$\chi^2/Z/t$ value	P value
Female/Male(case)	108/149	41/68	0.620	0.432
Age (years)[a]	59.00 (51.00, 69.00)	61.00 (54.00, 71.00)	1.796	0.072
Smoking history [n(%)]	82 (31.91)	37 (34.86)	0.150	0.703
BMI (kg/m²)[b]	24.71±2.99	24.86±3.07	0.430	0.667
SBP (mmHg)[b]	139.22±20.28	142.29±21.05	1.290	0.199
DBP (mmHg)[b]	81.86±14.28	83.63±13.87	1.110	0.270
BUN (mmol/L)[a]	5.38 (4.43, 6.54)	5.46 (4.53, 6.80)	0.697	0.486
SCr (μmol/L)[a]	64.10 (52.10, 73.45)	63.30 (49.15, 78.85)	0.078	0.938
SUA (μmol/L)[a]	280.00 (228.50, 338.50)	276.00 (231.25, 340.00)	0.654	0.513
FBG (mmol/L)[a]	7.65 (6.11, 9.73)	7.79 (6.03, 11.02)	0.876	0.381
TC (mmol/L)[a]	4.54 (3.64, 5.24)	4.15 (3.44, 5.12)	1.475	0.140
Triglycerides (mmol/L)[a]	1.52 (1.17, 2.38)	1.46 (1.08, 2.03)	1.249	0.212
HDL-C (mmol/L)[a]	1.21 (1.03, 1.44)	1.16 (0.95, 1.46)	0.961	0.337
LDL-C (mmol/L)[a]	2.32 (1.73, 2.92)	2.11 (1.41, 2.75)	1.684	0.092
Albumin (g/L)[a]	41.60 (39.20, 44.20)	38.30 (35.90, 40.85)	7.282	<0.001
HbA_{1C} (%)[a]	8.20 (6.70, 9.95)	9.40 (7.33, 10.85)	3.240	0.001
FINS (pmol/L)[a]	64.51 (38.59, 113.32)	71.64 (43.43, 123.15)	1.131	0.258
FCP (nmol/L)[a]	0.34 (0.22, 0.54)	0.34 (0.19, 0.57)	0.385	0.700
eGFR	98.96 (89.34, 108.38)	92.51 (83.27, 102.83)	3.149	0.002
WBC($\times10^9$/L)[a]	6.00 (4.97, 7.12)	5.86 (4.91, 7.21)	0.423	0.672
LYM($\times10^9$/L)[a]	1.78 (1.45, 2.23)	1.50 (1.26, 2.04)	3.464	<0.001
RBC ($\times10^{12}$/L)[a]	4.53 (4.10, 4.96)	4.35 (3.95, 4.71)	2.628	0.009
PLT ($\times10^9$/L)[a]	187.00 (149.00, 237.00)	168.00 (138.50, 210.50)	2.060	0.039
Hemoglobin (g/L)[b]	136.65±18.90	130.57±19.44	2.790	0.006
PNI[a]	50.55 (47.90, 54.38)	46.10 (43.55, 48.90)	7.621	<0.001

Note: [a] data were expressed as M (P_{25}, P_{75}); [b] data were expressed as $\bar{x} \pm s$. eGFR, mL/(min·1.73 m²).

2.2 Correlation analysis between PNI and various indicators in T2DM patients

The results of Spearman test showed that PNI in T2DM patients was positively correlated with serum uric acid (SUA), total cholesterol (TC), triglycerides, HDL-C, LDL-C, albumin, fasting C-peptide (FCP), white blood cell count (WBC), lymphocyte count (LYM), red blood cell count (RBC), platelet count (PLT), hemoglobin, and eGFR (P<0.05), and negatively correlated with HbA_{1C} (P<0.05). **[Table 2]**

2.3 Binary logistic regression analysis of influencing factors for RKFD in T2DM patients

Taking whether RKFD occurred in T2DM patients (assigned as: no=0, yes=1) as the dependent variable, and the indicators with statistically significant differences (P<0.05) in **Table 1** (assigned as: measured values) as independent variables, multivariate logistic regression analysis was performed. After collinearity diagnosis, PNI, HbA1C, hemoglobin, and PLT were included in the binary logistic regression analysis. The results showed that PNI and HbA_{1C} were independent influencing factors for RKFD in T2DM patients (P<0.05). **[Table 3]**

2.4 ROC Curve of PNI for predicting RKFD in T2DM patients

The ROC curve showed that the AUC of PNI for predicting RKFD in T2DM patients was 0.752 (95%CI: 0.699–0.805), with a cut-off value of 49.33, a sensitivity of 0.658, and a specificity of 0.789. **[Figure 1]**

Tab. 2 Correlation analysis between PNI and various indicators

Indicator	*r* value	*P* value	Indicator	*r* value	*P* value
BUN	0.004	0.937	**HbA_{1c}**	-0.163	0.002
SCr	0.067	0.202	**FINS**	-0.054	0.302
SUA	0.208	<0.001	**FCP**	0.177	0.001
FBG	-0.034	0.519	**WBC**	0.255	<0.001
TV	0.265	<0.001	**LYM**	0.638	<0.001
Triglycerides	0.284	<0.001	**RBC**	0.461	<0.001
HDL-C	0.119	0.023	**PLT**	0.150	0.004
LDL-C	0.126	0.016	**Hemoglobin**	0.507	<0.001
Albumin	0.851	<0.001	**eGFR**	0.224	<0.001

Tab. 3 Multivariate logistic regression analysis of rapid kidney function decline in T2DM patients

Item	*β* value	*SE* value	*Wald* χ^2 value	*P* value	*OR* value	*95% CI*
PNI	-0.167	0.030	30.909	<0.001	0.846	0.798-0.898
HbA_{1c}	0.114	0.054	4.488	0.034	1.121	1.009-1.247
Hemoglobin	0.005	0.008	0.383	0.536	1.005	0.990-1.020
RBC	-0.003	0.002	2.122	0.145	0.997	0.993-1.001
Intercept	6.137	1.405	19.071	<0.001	462.707	

3 Discussion

DKD is the leading cause of end-stage renal disease worldwide and a common microvascular complication of diabetes, with persistently high incidence and mortality

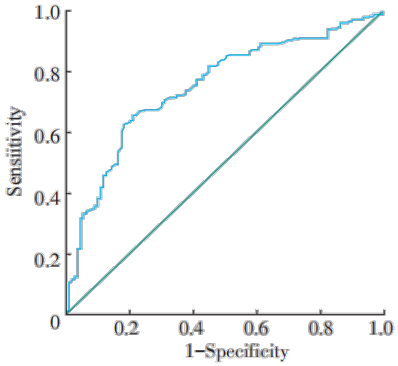

Fig.1 ROC curve for PNI predicting RKFD in T2DM patients

[15]. Patients with DKD, especially those with end-stage renal disease, are highly susceptible to malnutrition, which reduces quality of life and increases the risk of poor prognosis [16]. Studies have shown that early intervention in DKD can effectively prevent or delay the progression of renal failure and improve clinical outcomes [17]. Therefore, early identification of high-risk populations for RKFD in patients with T2DM is crucial for preventing DKD and developing personalized treatment strategies.

PNI reflects a patient's nutritional status, immune status, and inflammatory status. Low PNI is often associated with malnutrition and immunosuppression, factors that have been shown in multiple studies to be closely related to the deterioration of renal function [18-19]. Compared with serum albumin level or total lymphocyte count alone, PNI exhibits better predictive efficacy for mortality in patients undergoing renal dialysis [20]. PNI is also significantly associated with mortality in elderly patients with chronic kidney disease and has high predictive value [21]. In diabetic complications such as retinopathy, which shares similar pathological mechanisms with renal damage (especially microangiopathy), studies have shown that lower PNI values are common in T2DM patients with retinopathy and are closely associated with the development of retinopathy [22]. In this study, PNI levels in the RKFD group were lower than those in the non-RKFD group, indicating poorer nutritional and immune status in T2DM patients with RKFD. Spearman correlation analysis revealed that PNI was closely associated with renal function indices, glycemic and lipid metabolic indices, and inflammatory markers. Multivariate logistic regression analysis further confirmed that patients with lower PNI had a higher risk of developing RKFD, suggesting that low PNI may accelerate the deterioration of renal function through malnutrition and chronic inflammatory responses. ROC curve analysis showed that PNI had certain predictive value for RKFD in T2DM patients, with an AUC of 0.752 and an optimal cutoff value of 49.33. However, the optimal cutoff value of PNI may vary across populations, and thus patient-specific characteristics should be considered in clinical applications.

Although the prognostic value of PNI in other complications of T2DM has been reported [23-24], this study systematically verified the clinical predictive value of PNI in predicting RKFD in T2DM patients. This found that PNI is not only an important indicator of nutritional status but also an independent influencing factor for predicting renal function prognosis in T2DM patients. The predictive value of PNI may be exerted through the following mechanisms:

(1) Malnutrition and immunodeficiency: PNI combine serum albumin and peripheral blood lymphocyte levels, both of which are effective indicators of nutritional status and immune function. A low PNI indicates malnutrition and immunosuppression in patients. Long-term malnutrition may lead to glomerulosclerosis and renal interstitial fibrosis, accelerating the deterioration of renal function [24].

(2) Chronic inflammatory response: Low PNI is closely associated with systemic chronic inflammation, which plays a key role in the pathogenesis of T2DM and DKD [25]. Inflammatory responses cause renal tissue damage and impaired repair function, potentially accelerating the decline in renal function.

(3) Metabolic abnormalities and poor glycemic control: Low PNI is closely associated with metabolic abnormalities in diabetic patients, particularly poor glycemic control and lipid metabolism disorders. These metabolic disturbances further exacerbate renal damage by activating oxidative stress and forming advanced glycation end products [26-27]. In this study, decreased PNI levels and increased HbA_{1c} levels were independent risk factors for RKFD in T2DM patients, supporting this mechanism.

Thus, PNI is not only a reflection of nutritional status but also a comprehensive predictive indicator of renal function prognosis risk. Low PNI may contribute to the accelerated deterioration of renal function in T2DM patients through the combined effects of these complex pathological mechanisms.

In conclusion, PNI has certain clinical value in predicting RKFD in patients with T2DM. In clinical practice, more active nutritional intervention and chronic inflammation management should be implemented for patients with lower PNI to help prevent or slow further deterioration of renal function, thereby improving long-term prognosis. However, this study has limitations: first, as a retrospective study with a relatively short follow-up duration, unrecognized confounding factors may exist; second, dynamic changes in PNI were not included in the analysis, and future studies should further investigate the impact of temporal changes in PNI on renal function; third, this was a single-center study with a small sample size, leading to limited external validity. Therefore, future multicenter, large-sample prospective studies are needed to validate and optimize the application value of PNI in different T2DM populations.

Conflict of interest None

Reference

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·论 著·

预后营养指数对2型糖尿病患者肾功能快速下降的预测价值

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摘要：目的 探讨预后营养指数（PNI）在预测2型糖尿病（T2DM）患者肾功能变化中的作用。**方法** 回顾性选取2015年1月至2021年1月于芜湖市第一人民医院就诊的366例T2DM患者作为研究对象，治疗后进行随访，随访截至2024年8月。收集患者的临床资料，并计算患者估算肾小球滤过率（eGFR）年下降值，将患者分为肾功能快速下降（RKFD）组（n=109）和非RKFD组（n=257），RKFD定义为eGFR年下降值＞3 mL/（min·1.73 m^2）。采用Spearman相关性分析探究T2DM患者的PNI与各指标的相关性；通过多因素logistic回归分析T2DM患者RKFD的影响因素；运用受试者工作特征（ROC）曲线分析PNI的预测价值。**结果** 366例T2DM患者的中位随访时间为5年，共有109例（29.78%）患者发生RKFD。RKFD组基线糖化血红蛋白（HbA_{1c}）水平高于非RKFD组［9.40%（7.33%，10.85%）*vs* 8.20%（6.70%，9.95%），Z=3.240，P=0.001］，白蛋白、eGFR、淋巴细胞计数、红细胞计数、血小板计数、血红蛋白和PNI均低于非RKFD组（P<0.05）。Spearman相关性分析结果显示，T2DM患者PNI分别与尿酸、总胆固醇、三酰甘油、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、白蛋白、空腹C肽、白细胞计数、淋巴细胞计数、红细胞计数、血小板计数、血红蛋白、eGFR呈正相关（P<0.05），与HbA_{1c}呈负相关（r=−0.163，P=0.002）。多因素logistic回归分析显示，PNI（OR=0.846，95%CI：0.798~0.898，P＜0.01）和HbA_{1c}（OR=1.121，95%CI：1.009~1.247，P=0.034）为发生RKFD的独立影响因素。ROC曲线分析显示，PNI预测T2DM患者发生RKFD的曲线下面积为0.752，截断值为49.33，灵敏度为0.658，特异度为0.789。**结论** PNI较低的T2DM患者发生RKFD的风险更高，PNI可作为评估T2DM患者肾功能预后风险的重要指标。

关键词： 预后营养指数；2型糖尿病；肾功能快速下降；糖尿病肾病；肾小球滤过率；糖化血红蛋白
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Predictive value of the prognostic nutritional index for rapid kidney function decline in patients with type 2 diabetes mellitus

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Abstract: Objective To investigate the role of the prognostic nutritional index (PNI) in predicting renal function changes in patients with type 2 diabetes mellitus (T2DM). **Methods** A retrospective study was conducted with 366 T2DM patients who visited the First People's Hospital of Wuhu from January 2015 to January 2021. Follow-up was performed after treatment, with the final follow-up in August 2024. Clinical data were collected, and the annual decline in the estimated glomerular filtration rate (eGFR) was calculated. Patients were divided into two groups: the rapid kidney function decline (RKFD) group (n=109) and the non-RKFD group (n=257), with RKFD defined as an annual eGFR decline over 3 mL/(min·1.73 m^2). Spearman correlation analysis was used to explore the relationship between

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PNI and various indicators in T2DM patients. Multivariate logistic regression analysis was performed to identify the factors influencing RKFD in T2DM patients. The predictive value of PNI was evaluated using receiver operating characteristic (ROC) curves. **Results** The median follow-up period for the 366 T2DM patients was 5 years, with 109 (29.78%) patients experiencing RKFD. The baseline level of glycated hemoglobin (HbA_{1C}) in the RKFD group was higher than that in the non-RKFD group [9.40% (7.33%, 10.85%) *vs* 8.20% (6.70%, 9.95%), Z=3.240, P=0.001]. Compared with non-RKFD group, the albumin, eGFR, lymphocyte count, red blood cell count, platelet count, hemoglobin, and PNI were lower in the RKFD group (P<0.05). Spearman correlation analysis showed that PNI in T2DM patients was positively correlated with uric acid, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, albumin, fasting C-peptide, white blood cell count, lymphocyte count, red blood cell count, platelet count, hemoglobin, and eGFR, respectively (P<0.05), and was negatively correlated with HbA_{1C} (r=−0.163, P=0.002). Multivariate logistic regression analysis indicated that independent factors influencing RKFD included PNI (OR=0.846, 95% CI: 0.798−0.898, P<0.01) and HbA_{1C} (OR=1.121, 95% CI: 1.009−1.247, P=0.034). ROC curve analysis showed that the area under the curve for PNI in predicting RKFD in T2DM patients was 0.752, with an optimal cut-off value of 49.33, sensitivity of 0.658, and specificity of 0.789. **Conclusion** T2DM patients with lower PNI are at higher risk of RKFD, and PNI can be served as an important indicator for assessing the renal function prognosis in T2DM patients.

Keywords: Prognostic nutritional index; Type 2 diabetes mellitus; Rapid kidney function decline; Diabetic kidney disease; Glomerular filtration rate; Glycated hemoglobin

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2型糖尿病(type 2 diabetes mellitus, T2DM)是全球范围内常见的慢性代谢性疾病,其发病率和患病率逐年上升[1-2]。流行病学研究表明,约40%的糖尿病患者最终发展为糖尿病肾病(diabetic kidney disease, DKD)[3]。DKD是终末期肾病的主要病因,严重影响患者的生存质量和预后[4]。DKD的发展初期通常无显著症状,仅表现为轻度蛋白尿,而且早期肾功能下降缺乏有效生物标志物进行准确预测,使得早期诊断困难[5-6]。尽管血糖控制、血压管理及肾素-血管紧张素系统抑制等干预措施能够减缓DKD的进展,但仍有相当一部分T2DM患者出现肾功能快速下降(rapid kidney function decline, RKFD)[7]。近年来,人们一直关注生活方式因素和营养状况对T2DM的影响。预后营养指数(prognostic nutritional index,PNI)作为评价患者营养状态的重要指标,已被广泛应用于评估肿瘤、心血管疾病和慢性肾脏病等多种疾病的预后[8-9]。低水平的PNI往往提示营养不良和免疫功能低下[10]。PNI已被证实在T2DM患者并发症的不良心血管事件中具有重要的临床预测价值[11]。然而,目前PNI对T2DM患者RKFD的预测价值研究较少,本研究旨在探讨PNI水平对T2DM患者RKFD的预测价值,以期分析PNI在预测T2DM患者肾功能变化中的作用。

1 资料与方法

1.1 一般资料 回顾性选取2015年1月至2021年1月于芜湖市第一人民医院就诊的366例T2DM患者作为研究对象。本研究经芜湖市第一人民医院医学伦理委员会审批通过(批号:YYLL20230046)。纳入标准:(1)符合1999年WHO制订的有关T2DM的诊断标准;(2)年龄≥18岁;(3)首次就诊时估算肾小球滤过率(estimated glomerular filtration rate, eGFR)≥60 mL/(min·1.73 m^2);(4)至少有1次有效随访,必须包括空腹血清肌酐检测;(5)临床资料完整。排除标准:(1)合并急性肾损伤、其他因素引起的肾脏疾病、尿路感染;(2)哺乳或妊娠期;(3)1型糖尿病、妊娠期糖尿病等其他糖尿病;(4)糖尿病酮症酸中毒、高渗性昏迷等严重急性并发症;(5)合并恶性肿瘤、严重感染等重大疾病;(6)合并心、肝等严重脏器疾病。

1.2 *方法*

1.2.1 资料收集 (1)基线资料:包括性别、年龄、收缩压、舒张压等。(2)首次就诊时血液指标:包括血常规、白蛋白、血尿素氮、血肌酐、血尿酸、空腹血糖、总胆固醇、三酰甘油、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、糖化血红蛋白(glycated hemoglobin, HbA_{1C})、空腹胰岛素(fasting insulin, FINS)、空腹C肽,并计算eGFR和PNI值。(3)随访资料:随访截止时间为2024年8月,每次的门诊或住院诊疗为1次有效随访,且2次有效随访时间间隔大于1年,随访方式为查阅门诊或住院电子

病历系统病案。收集患者末次门诊或住院的空腹血清肌酐值并计算eGFR值和年度eGFR下降值。PNI计算公式[12]：PNI=血清白蛋白(g/L)+5×外周血淋巴细胞计数(×10⁹/L)；采用慢性肾脏病流行病学合作研究(Chronic Kidney Disease Epidemiology Collaboration，CKD-EPI)公式计算eGFR[13]。

1.2.2　入组定义　患者根据肾功能是否快速下降分为非RKFD组和RKFD组，RKFD定义为平均每年eGFR下降值＞3 mL/(min·1.73 m²)[14]。通过受试者工作特征(receiver operator characteristic，ROC)曲线分析确定PNI预测RKFD的截断值。

1.3　统计学方法　采用SPSS 27.0统计软件进行数据分析。分类变量以例(%)表示，组间比较采用χ^2检验。符合正态分布的连续变量以$\bar{x}\pm s$表示，组间比较采用独立样本t检验，非正态分布的连续变量以$M(P_{25}, P_{75})$表示，两组间的差异性分析采用Mann-Whitney U检验。PNI与各指标间的相关性采用Spearman相关性分析。采用多因素logistic回归分析探讨T2DM患者RKFD的影响因素，并绘制ROC曲线，计算PNI预测RKFD的曲线下面积(area under curve，AUC)、灵敏度和特异度及其95%CI。P<0.05为差异有统计学意义。

2　结　果

2.1　两组患者基线资料比较　本研究共纳入366例T2DM患者，中位随访期为5年，其中109例患者发生RKFD，发生率为29.78%(109/366)。基线资料分析显示，RKFD组HbA_{1C}水平高于非RKFD组，白蛋白、eGFR、淋巴细胞计数、红细胞计数、血小板计数、血红蛋白和PNI均低于非RKFD组(P<0.05)。两组患者性别、年龄及其余指标差异均无统计学意义(P>0.05)。见表1。

2.2　T2DM患者PNI与各指标的相关性分析　采用Spearman检验分析结果显示，T2DM患者PNI与血尿酸、总胆固醇、三酰甘油、HDL-C、LDL-C、白蛋白、空腹C肽、白细胞计数、淋巴细胞计数、红细胞计数、血小板计数、血红蛋白、eGFR呈正相关(P<0.05)，与HbA_{1C}呈负相关(P<0.05)。见表2。

2.3　二元logistic回归分析T2DM患者发生RKFD的影响因素　以T2DM患者是否发生RKFD(赋值：否=0，是=1)为因变量，将表1中差异有统计学意义(P<0.05)的指标(赋值：实测值)作为自变量进行多因素

表1　非RKFD组与RKFD组基线资料比较

Tab.1　Comparison of baseline characteristics between non-RKFD group and RKFD group

项目	非RKFD组(n=257)	RKFD组(n=109)	$\chi^2/Z/t$值	P值
性别(女/男，例)	108/149	41/68	0.620	0.432
年龄(岁)[a]	59.00 (51.00, 69.00)	61.00 (54.00, 71.00)	1.796	0.072
吸烟史[例(%)]	82(31.91)	37(34.86)	0.150	0.703
身体质量指数(kg/m²)[b]	24.71±2.99	24.86±3.07	0.430	0.667
收缩压(mmHg)[b]	139.22±20.28	142.29±21.05	1.290	0.199
舒张压(mmHg)[b]	81.86±14.28	83.63±13.87	1.110	0.270
血尿素氮(mmol/L)[a]	5.38(4.43, 6.54)	5.46(4.53, 6.80)	0.697	0.486
血肌酐(μmol/L)[a]	64.10 (52.10, 73.45)	63.30 (49.15, 78.85)	0.078	0.938
血尿酸(μmol/L)[a]	280.00 (228.50, 338.50)	276.00 (231.25, 340.00)	0.654	0.513
空腹血糖(mmol/L)[a]	7.65 (6.11, 9.73)	7.79 (6.03, 11.02)	0.876	0.381
总胆固醇(mmol/L)[a]	4.54 (3.64, 5.24)	4.15 (3.44, 5.12)	1.475	0.140
三酰甘油(mmol/L)[a]	1.52 (1.17, 2.38)	1.46 (1.08, 2.03)	1.249	0.212
HDL-C(mmol/L)[a]	1.21 (1.03, 1.44)	1.16 (0.95, 1.46)	0.961	0.337
LDL-C(mmol/L)[a]	2.32 (1.73, 2.92)	2.11 (1.41, 2.75)	1.684	0.092
白蛋白(g/L)[a]	41.60 (39.20, 44.20)	38.30 (35.90, 40.85)	7.282	<0.001
HbA_{1C}(%)[a]	8.20 (6.70, 9.95)	9.40 (7.33, 10.85)	3.240	0.001
FINS(pmol/L)[a]	64.51 (38.59, 113.32)	71.64 (43.43, 123.15)	1.131	0.258
空腹C肽(nmol/L)[a]	0.34 (0.22, 0.54)	0.34 (0.19, 0.57)	0.385	0.700
eGFR[mL/(min·1.73 m²)][a]	98.96(89.34, 108.38)	92.51(83.27, 102.83)	3.149	0.002
白细胞计数(×10⁹/L)[a]	6.00(4.97, 7.12)	5.86(4.91,7.21)	0.423	0.672
淋巴细胞计数(×10⁹/L)[a]	1.78(1.45, 2.23)	1.50 (1.26, 2.04)	3.464	<0.001
红细胞计数(×10¹²/L)[a]	4.53 (4.10, 4.96)	4.35 (3.95, 4.71)	2.628	0.009
血小板计数(×10⁹/L)[a]	187.00 (149.00, 237.00)	168.00 (138.50, 210.50)	2.060	0.039
血红蛋白(g/L)[b]	136.65±18.90	130.57±19.44	2.790	0.006
PNI[a]	50.55 (47.90, 54.38)	46.10 (43.55, 48.90)	7.621	<0.001

注：[a]数据用$M(P_{25}, P_{75})$表示；[b]数据用$\bar{x}\pm s$表示。

logistic 回归分析，经过共线性诊断，将 PNI、HbA_{1C}、血红蛋白和血小板计数纳入二元 logistic 回归分析，结果显示，PNI 和 HbA_{1C} 为 T2DM 患者发生 RKFD 的独立影响因素（P<0.05）。见表 3。

2.4　PNI 预测 T2DM 患者 RKFD 的 ROC 曲线　ROC 曲线显示，PNI 预测 T2DM 患者发生 RKFD 的 AUC 为 0.752（95%*CI*：0.699～0.805），截断值为 49.33，灵敏度为 0.658，特异度为 0.789。见图 1。

表 2　PNI 与各指标的相关性分析

Tab.2　Correlation analysis between PNI and various indicators

指标	r 值	P 值	指标	r 值	P 值
血尿素氮	0.004	0.937	HbA_{1C}	−0.163	0.002
血肌酐	0.067	0.202	FINS	−0.054	0.302
血尿酸	0.208	<0.001	空腹 C 肽	0.177	0.001
空腹血糖	−0.034	0.519	白细胞计数	0.255	<0.001
总胆固醇	0.265	<0.001	淋巴细胞计数	0.638	<0.001
三酰甘油	0.284	<0.001	红细胞计数	0.461	<0.001
HDL-C	0.119	0.023	血小板计数	0.150	0.004
LDL-C	0.126	0.016	血红蛋白	0.507	<0.001
白蛋白	0.851	<0.001	eGFR	0.224	<0.001

表 3　T2DM 患者发生 RKFD 的多因素 logistic 回归分析

Tab.3　Multivariate logistic regression analysis of RKFD in T2DM patients

自变量	β 值	SE 值	Wald 值	P 值	OR 值	95% CI
PNI	−0.167	0.030	30.909	<0.001	0.846	0.798～0.898
HbA_{1C}	0.114	0.054	4.488	0.034	1.121	1.009～1.247
血红蛋白	0.005	0.008	0.383	0.536	1.005	0.990～1.020
血小板计数	−0.003	0.002	2.122	0.145	0.997	0.993～1.001
常量	6.137	1.405	19.071	<0.001	462.707	

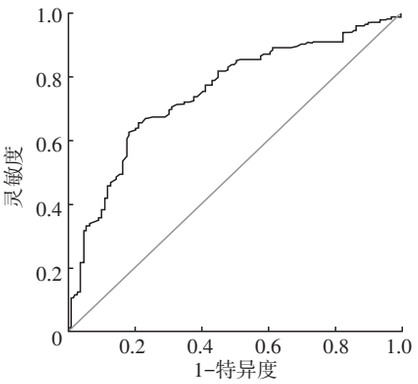

图 1　PNI 预测 T2DM 患者 RKFD 的 ROC 曲线

Fig.1　ROC curve for PNI predicting RKFD in T2DM patients

3　讨　论

DKD 是全球终末期肾病的主要病因，也是糖尿病常见的微血管并发症，其发病率及死亡率居高不下[15]。DKD 患者，尤其是终末期肾病患者，极易营养不良，导致生活质量下降，预后恶化的风险增加[16]。研究表明，DKD 的早期干预可以有效预防或延缓肾衰竭的进展，改善患者的临床结局[17]。因此，在 T2DM 患者中早期识别 RKFD 的高危人群，对于预防 DKD 和制定个性化治疗方案至关重要。

PNI 反映患者的营养状况、免疫状况和炎症状况，低 PNI 常伴随营养不良和免疫抑制，而这些因素已被多项研究证明与肾功能的恶化密切相关[18-19]。与单独的血清白蛋白水平或总淋巴细胞计数相比，PNI 对肾透析患者显示出更好的死亡率预测效能[20]。PNI 与老年慢性肾病患者死亡率亦显著相关，且具有较高的预测价值[21]。在糖尿病并发症（如视网膜病变）中，其与肾脏损害有相似的病理机制，尤其是微血管病变。有研究显示，较低的 PNI 值在 T2DM 患者并发视网膜病变中很常见，并与视网膜病变的发生密切相关[22]。在本研究中，RKFD 组 PNI 水平低于非 RKFD，表明 T2DM 患者营养和免疫状态较差。Spearman 相关性研究显示，PNI 与肾功能指标、血糖血脂代谢指标及炎症指标密切相关。多因素 logistic 回归分析进一步证实，PNI 较低患者发生 RKFD 的风险更高，表明低 PNI 可能通过营养不良和慢性炎症反应加速肾功能的恶化。ROC 曲线分析结果显示，PNI 对 T2DM 患者发生 RKFD 具有一定的预测价值，AUC 为 0.752，截断值为 49.33。然而，PNI 在不同人群中的截断值可能存在差异，因此在临床应用中应考虑患者的个体特征。

尽管 PNI 在 T2DM 患者其他并发症中预后评估价值已有报道[23]，但本研究系统性验证了 PNI 在预测 T2DM 患者 RKFD 中的临床预测价值。笔者发现 PNI 不仅是评价营养状况的重要指标，也是预测 T2DM 患者肾功能预后的独立影响因素。PNI 的预测价值可能通过以下机制发挥作用。（1）营养不良与免疫功能低下：PNI 结合了血清白蛋白和外周血淋巴细胞的水平，这两者均是营养状况和免疫功能的有效指标。PNI 水平较低提示患者存在营养不良和免疫抑制状态，长期营养不良可能导致肾小球硬化和肾间质纤维化，加速肾功能的恶化[24]。（2）慢性炎症反应：低 PNI 与全身性慢性炎症状态密切相关，而慢性炎症在 T2DM 和 DKD 的发病过程中扮演重要角色[25]。炎症反应导致肾脏组织损伤及修复功能障碍，可能加速肾功能的下降。（3）代谢异常与高血糖控制不佳：低 PNI 与糖尿病患者的代谢异常密切相关，特别是血糖控制不良与脂质代谢紊乱，这些代谢紊乱通过激活氧化应激和形成糖基化终产物，进一步加重了肾脏损伤[26-27]。在本研究中，PNI 水平的降低和 HbA_{1C} 水平的升高作为 T2DM 患者 RKFD 的独立危险

因素，支持了这一机制。因此，PNI不仅是营养状态的反映，更是肾功能预后风险的综合预测指标，低PNI可能通过这些复杂的病理机制共同作用，导致T2DM患者肾功能的加速恶化。

综上所述，PNI在预测T2DM患者RKFD中具有一定的临床价值。在临床实践中，对PNI较低的患者应采取更积极的营养干预和慢性炎症管理，有助于预防或减缓肾功能的进一步恶化，从而改善患者的长期预后。然而，本研究也存在一定局限性：首先，作为一项回顾性研究，随访时间相对较短，可能存在未被识别的混杂因素；其次，PNI的动态变化未被纳入分析，未来应进一步研究PNI随时间变化对肾功能的影响；此外，本研究为单中心小样本量研究，外部效度有限。因此，今后应开展多中心、大样本的前瞻性研究来验证和优化PNI在不同T2DM人群中的应用价值。

利益冲突　无

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