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# Serum Podoplanin Levels as a Potential Biomarker for Diabetic Nephropathy Progression: A Cross-Sectional Study

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**Objective:** The study aimed to investigate the impact of serum Podoplanin levels on diabetic nephropathy in patients with type 2 diabetes mellitus (T2DM).

**Patients and methods:** Between January 2022 and December 2023, the Department of Nephrology at Nantong Second People's Hospital selected 276 patients with T2DM and 150 healthy controls for this investigation. Systematic data collection was performed to gather information on biomarkers and biochemical parameters.

**Results:** When T2DM patients (n=276) and healthy controls (n=150) were compared, considerably lowered serum Podoplanin levels were observed. In all 276 patients, serum Podoplanin levels were negatively associated with age (r=−0.127, P=0.035), body mass index (BMI) (r=−0.292, P<0.001), duration of diabetes (r=−0.323, P<0.001), systolic blood pressure (SBP) (r=−0.255, P<0.001), diastolic blood pressure (DBP) (r=−0.138, P=0.022), fasting blood glucose (FBG) (r=−0.196, P=0.001), glycated hemoglobin (HbA1c) (r=−0.095, P=0.117), triglyceride (TG) (r=−0.157, P=0.009), total cholesterol (TC) (r=−0.126, P=0.036), low-density lipoprotein cholesterol (LDL-C) (r=−0.187, P=0.002), serum creatinine (Scr) (r=−0.500, P<0.001), neutrophil gelatinase-associated lipocalin (NGAL) (r=−0.339, P<0.001), and kidney injury molecule-1 (KIM-1) (r=−0.568, P<0.001), and was positively correlated with high-density lipoprotein cholesterol (HDL-C) (r=0.343, P<0.001) and estimated glomerular filtration rate (eGFR) (r=0.442, P<0.001). The multivariate logistic regression analysis showed that diabetic patients with DN had lowered levels of serum Podoplanin (OR=0.022, 95% CI=0.005–0.100; P<0.001), lower SBP, Scr, NGAL, and KIM-1.

**Conclusion:** The results indicated that diabetic patients with DN have lower levels of serum Podoplanin. A more considerable population-based prospective investigation is essential to validate our findings.

**Keywords:** podoplanin, type 2 diabetes mellitus, diabetic nephropathy, biomarker

## Introduction

Diabetic nephropathy (DN), also known as diabetic kidney disease (DKD), is a significant microvascular complication associated with diabetes mellitus (DM).[1,2] The progression of DN typically begins with the onset of hyperglycemia. It advances from a state of low-grade renal inflammation to more severe conditions, such as renal fibrosis and renal sclerosis. Ultimately, this progression may lead to end-stage renal disease (ESRD).[3] At this stage, patients often require either dialysis or kidney transplantation.[4] The implications of DN impose a substantial burden on public health, with its global prevalence and severe health consequences impacting communities worldwide.[5] Therefore, the international healthcare community needs to understand and address this pressing issue.

According to traditional descriptions of DN, various histopathological changes can be observed in the renal tissues of affected individuals. In the glomeruli, common findings include expansions of the capillary lumens, increased thickness of the basement membrane, expansion of the extracellular matrix, damage to podocytes, and the presence of fibrosis. Features such as vacuolar degeneration, disordered cellular arrangement, and fibrosis are frequently noted in the

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tubulointerstitial area.[6–8] As DN progresses, patients are often diagnosed with glomerular hyperfiltration, microproteinuria, macroproteinuria, and a reduced glomerular filtration rate (GFR).[9] The measurement of urinary protein (UP) is considered the primary metric for the clinical diagnosis of DN; this includes the urinary albumin excretion rate (UAER) in patients with microproteinuria and the 24-hour urinary protein collection for those with macroproteinuria.[10] Additional parameters may consist of assessments of renal function, blood glucose and lipid levels, and a comprehensive evaluation of any associated symptoms.[10]

Breiteneder-Geleff et al initially identified Podoplanin, a transmembrane glycoprotein expressed on podocytes, in the context of puromycin aminonucleoside nephrosis (PAN), a rat model that mimics human minimal change nephropathy.[11] Their investigation revealed that the expression levels of Podoplanin were significantly diminished by 70% in PAN characterized by the marked flattening of podocyte foot processes and pronounced proteinuria. Further research indicated that administering a single dose of anti-Podoplanin IgG in rats could elicit selective proteinuria, which was concomitantly associated with flattening foot processes.[12] Zhang et al additionally demonstrated that osteocyte E11/gp38, encoded by the same gene as Podoplanin, has a direct role in the dendritic formation of osteocyte-like cells.[13] Consequently, it is hypothesized that Podoplanin is integral to the preservation of the normal morphology and functional integrity of podocytes. However, the effect of Podoplanin on diabetic nephropathy in T2DM patients remains unknown. Therefore, in this study, we explored the clinical significance of serum Podoplanin for the differential diagnosis of diabetic nephropathy and healthy controls in patients with T2DM.

# Methods

## Study Population

In this cross-sectional study, we recruited 276 T2DM patients admitted to the Department of Nephrology at Nantong Second People's Hospital between January 2022 and December 2023. T2DM was diagnosed according to the following criteria: fasting glucose≥7.0 mmol/L or 2-h postprandial glucose level ≥11.1 mmol/L. All these 276 T2DM patients were divided into three subgroups: normoalbuminuria (urine albumin to creatinine ratio (ACR) < 30 mg/g) (n = 113), microalbuminuria (30 ≤ ACR ≤300 mg/g) (n = 95), and macroalbuminuria (ACR > 300 mg/g) (n = 68). DN was diagnosed when ACR > 30 mg/g. We also selected 150 subjects who went on routing health examination as the control group, and they matched age and gender. We excluded subjects with type 1 diabetes, a history of malignancy, and the existence of infectious, haematological or cardiovascular disorders. The Research Ethics Committee of Nantong Second People's Hospital approved this study protocol. Informed consent was obtained from participants.

## Measurement of Clinical and Biochemical Data

The general clinical data of patients were collected through inquiry with all subjects after admission, including age, gender, height, weight, T2DM duration, and blood pressure. BMI is expressed as weight per square meter (kg/m2). Fasting blood glucose (FBG) was determined by the glucose oxidase method. Glycosylated hemoglobin (HbA1c) was determined by high-performance liquid chromatography (HPLC). Blood lipid profile, including triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), and serum creatinine (Scr) were measured by a biochemistry automatic analyzer (Hitachi 7170, Tokyo, Japan). Renal function was assessed by eGFR using the simplified formula as follows: (mL/min/1.73 $m^2$) = 175 × {Scr (μmol/L)/88.4}-1.154 × (age)-0.203 × (if female).

## ELISA Assay

Blood samples were collected within 24 hours after admission, and the sample was collected in a sterile EDTA-coated tube. The serum was separated by centrifugation of 1500 g for 30 min and stored at −80°C. ELISA kit for NGAL (QK1757, R&D Systems), KIM-1 (DSKM100, R&D Systems) and antibodies of Podoplanin (AF3670, R&D Systems) measured serum biomarker levels in control subjects and T2DM patients. The absorbance at 450 nm was measured with a microplate reader. The concentrations of these proteins were calculated according to the standard curve.

## Statistical Analysis

SPSS20.0 statistical software was used for data processing and figure plotting. Data are displayed as mean ± standard deviation (SD) for continuous variables and as frequency (percentage) for categorical variables. The differences between the control and T2DM groups were determined using a *t*-test. The differences between the three subgroups of T2DM were determined using one-way ANOVA (customarily distributed numerical data) or the Kruskal–Wallis test. Categorical variables were analyzed using the chi-square test. The Pearson correlation analysis evaluated the correlation between Podoplanin and other clinical indicators. The independent influencing factors of Podoplanin were determined by univariate and multivariate logistic regression analysis. The ROC curve was made to determine the cut-off point of serum Podoplanin between T2DM patients with and without albuminuria. $P<0.05$ was considered as a criterion for a significant difference.

# Results

## Baseline Characteristics of the Study

The study compared T2DM and the control group using a comprehensive approach. The results of the Student's *t*-test showed that T2DM patients had higher levels of body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood glucose (FBG), glycated hemoglobin (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), serum creatinine (Scr), neutrophil gelatinase-associated lipocalin (NGAL), and kidney injury molecule-1 (KIM-1) while eGFR and Podoplanin levels were lower in T2DM patients (Table 1). However, about age, gender, and triglyceride (TG) ($P > 0.05$), there were no significant differences between the T2DM and control groups.

In addition, we compared all subgroups of T2DM using Student's *t*-test approach, and the results demonstrated that the macroalbuminuria subgroup had higher levels of BMI, SBP, DBP, FPG, TC, LDL-C, Scr, NGAL, and KIM-1 compared to microalbuminuria and normoalbuminuria (Table 2). On the other hand, HDL-C, eGFR, and Podoplanin

**Table 1** Baseline Characteristics of the Study Population

| Characteristics | Control (n = 150) | T2DM (n = 276) | P-Value |
|---|---|---|---|
| Age (years) | 55.89±10.19 | 55.70±10.20 | 0.848 |
| Gender (male, %) | 82 (54.7%) | 147 (53.3%) | 0.781 |
| BMI (kg/m$^2$) | 24.05±1.26 | 24.57±1.28 | <0.001 |
| Duration (years) | 0 | 9.29±1.98 | <0.001 |
| SBP (mmHg) | 123.45±10.91 | 138.86±15.76 | <0.001 |
| DBP (mmHg) | 77.88±7.09 | 86.75±13.31 | <0.001 |
| FPG (mmol/L) | 4.73±0.65 | 7.78±1.15 | <0.001 |
| HbA1c (%) | 4.95±0.81 | 7.96±1.22 | <0.001 |
| TG (mmol/L) | 1.92±0.79 | 2.13±0.84 | 0.10 |
| TC (mmol/L) | 5.28±0.49 | 5.51±0.72 | <0.001 |
| LDL-C (mmol/L) | 3.14±0.48 | 3.52±0.55 | <0.001 |
| HDL-C (mmol/L) | 1.51±0.22 | 1.17±0.21 | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 103.91±19.71 | 98.21±21.77 | 0.008 |
| Scr (μmol/L) | 68.01±10.60 | 83.48±17.83 | <0.001 |
| NGAL (μg/mL) | 83.72±16.75 | 132.33±30.18 | <0.001 |
| KIM-1 (ng/mL) | 12.51±2.37 | 23.45±5.52 | <0.001 |
| Podoplanin (ng/mL) | 5.54±0.73 | 3.30±0.69 | <0.001 |

**Notes**: Continuous variables are expressed as mean ± SD, and analyzed using *t* test or Wilcoxon-Mann–Whitney test. Categorical variables are expressed as frequency (percentage), and analyzed using the chi-square test.

**Abbreviations**: CAD, coronary artery disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; HbA1c, glycated haemoglobin; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; Scr, serum creatinine; NGAL, neutrophil gelatinase-associated lipocalin; KIM-1, kidney injury molecule-1.

**Table 2** Baseline Characteristics Between All Subgroups of T2DM

| Characteristics | Normoalbuminuria (n = 113) | Microalbuminuria (n = 95) | Macroalbuminuria (n = 68) | P-Value |
|---|---|---|---|---|
| Age (years) | 52.68±9.42 | 56.45±10.09 | 59.65±10.19 | <0.001 |
| Gender (male, %) | 56 (49.6%) | 91 (55.8%) | 147 (53.3%) | 0.305 |
| BMI (kg/m$^2$) | 24.02±1.16 | 24.68±1.18 | 25.32±1.22 | <0.001 |
| Duration (years) | 8.11±1.38 | 9.54±1.77 | 10.91±1.84 | <0.001 |
| SBP (mmHg) | 130.85±13.25 | 142.23±14.44 | 147.47±15.28 | <0.001 |
| DBP (mmHg) | 81.35±11.48 | 89.11±12.92 | 92.46±13.53 | <0.001 |
| FPG (mmol/L) | 7.47±1.04 | 7.76±0.92 | 8.34±1.40 | <0.001 |
| HbA1c (%) | 7.68±1.01 | 8.09±1.38 | 8.22±1.22 | 0.006 |
| TG (mmol/L) | 1.91±0.76 | 2.26±0.88 | 2.32±0.81 | 0.001 |
| TC (mmol/L) | 5.31±0.68 | 5.60±0.70 | 5.73±0.75 | <0.001 |
| LDL-C (mmol/L) | 3.31±0.44 | 3.59±0.49 | 3.75±0.68 | <0.001 |
| HDL-C (mmol/L) | 1.27±0.18 | 1.17±0.20 | 1.02±0.17 | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 110.84±22.45 | 98.30±12.54 | 77.08±12.68 | <0.001 |
| Scr (μmol/L) | 72.36±9.35 | 82.04±13.35 | 103.98±16.44 | <0.001 |
| NGAL (μg/mL) | 112.91±21.16 | 137.76±25.26 | 157.03±28.22 | <0.001 |
| KIM-1 (ng/mL) | 19.51±2.73 | 22.73±3.41 | 31.01±3.35 | <0.001 |
| Podoplanin (ng/mL) | 3.80±0.53 | 3.28±0.47 | 2.52±0.42 | <0.001 |

levels were lowered in the macroalbuminuria subgroup. This comprehensive investigation provides a solid basis for further research and clinical practice.

## Serum Podoplanin Levels in T2DM Patients

The serum Podoplanin levels in T2DM patients (n=276) and healthy controls (n=150) underwent ELISA testing. The serum concentration of Podoplanin in T2DM patients was significantly lower than that in healthy controls (Figure 1A). In addition, we compared the serum Podoplanin levels between normoalbuminuria (n=113), microalbuminuria (n=95), and macroalbuminuria (n=68) and observed significantly reduced Podoplanin levels in microalbuminuria and macroalbuminuria than normoalbuminuria (Figure 1B). However, the T2DM group (3.30±0.69 ng/mL) showed markedly lower serum Podoplanin levels than the healthy control (5.54±0.73 ng/mL) (Table 1).

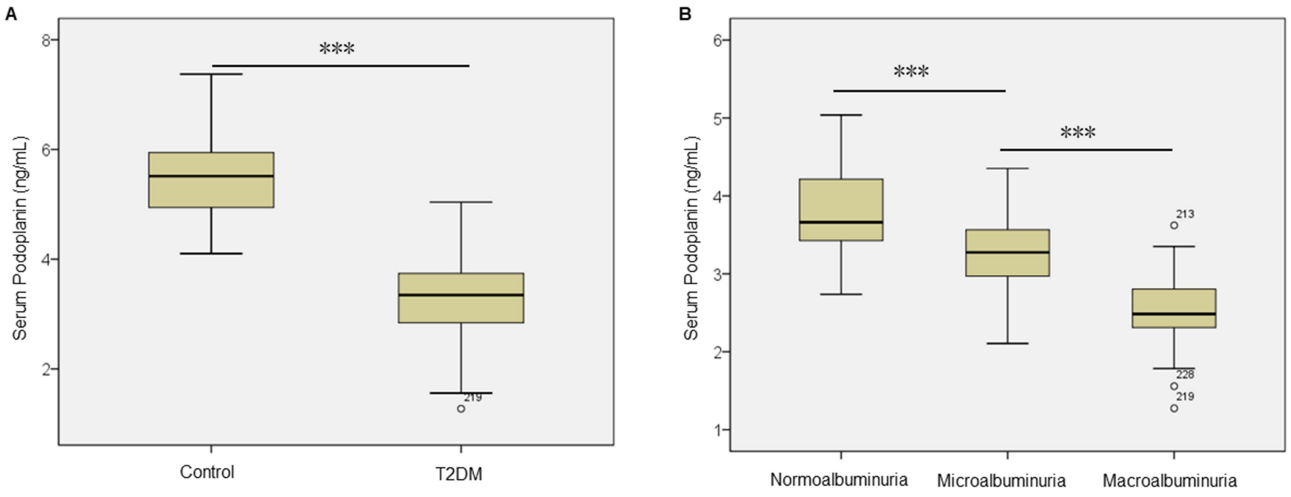


**Figure 1** Serum Podoplanin levels in control subjects and T2DM patients. (**A**) Comparison of serum Podoplanin levels between control subjects and T2DM patients. The serum Podoplanin concentration in T2DM patients (n = 276) was significantly lower than that in control subjects (n = 150). *T* test was applied. (**B**) Comparison of serum Podoplanin levels in three subgroups of T2DM patients. ANOVA was applied. ***P<0.001.

**Table 3** Correlation Between Serum Podoplanin and Clinical Indicators

| Parameters | All Subjects (n=293) | |
|---|---|---|
| | r | P |
| Age (years) | −0.127 | 0.035 |
| BMI (kg/m$^2$) | −0.292 | <0.001 |
| Duration (years) | −0.323 | <0.001 |
| SBP (mmHg) | −0.255 | <0.001 |
| DBP (mmHg) | −0.138 | 0.022 |
| FPG (mmol/L) | −0.196 | 0.001 |
| HbA1c (%) | −0.095 | 0.117 |
| TG (mmol/L) | −0.157 | 0.009 |
| TC (mmol/L) | −0.126 | 0.036 |
| LDL-C (mmol/L) | −0.187 | 0.002 |
| HDL-C (mmol/L) | 0.343 | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 0.442 | <0.001 |
| Scr (μmol/L) | −0.500 | <0.001 |
| NGAL (μg/mL) | −0.339 | <0.001 |
| KIM-1 (ng/mL) | −0.568 | <0.001 |

**Notes**: The correlation between serum Podoplanin and other continuous variables was analyzed using the Pearson correlation test.

## Correlation Between Serum Podoplanin and Clinical Indicators

In all 276 T2DM patients, negatively associated serum Podoplanin levels with age (r=−0.127, P=0.035), BMI (r=−0.292, P<0.001), duration (r=−0.323, P<0.001), SBP (r=−0.255, P<0.001), DBP (r=−0.138, P=0.022), FPG (r=−0.196, P=0.001), HbA1c (r=−0.095, P=0.117), TG (r=−0.157, P=0.009), TC (r=−0.126, P=0.036), LDL-C (r=−0.187, P=0.002), Scr (r=−0.500, P<0.001), NGAL (r=−0.339, P<0.001), and KIM-1 (r=−0.568, P<0.001), and was positively associated with HDL-C (r=0.343, P<0.001) and eGFR (r=0.442, P<0.001) (Table 3). In addition, Podoplanin was correlated with eGFR, Scr, NGAL, and KIM-1 using a Pearson correlation test. The results showed that the serum Podoplanin levels were negatively correlated with Scr, NGAL, and KIM-1, while eGFR was positively correlated with Podoplanin levels (Figure 2).

## Logistic Regression Analysis for Developing DN

Univariate and multivariate logistic regression analyses were performed to identify independent risk variables of DN. The univariate logistic regression analysis results showed that Scr (OR=1.084, 95% CI=1.014–1.157; P=0.017), NGAL (OR=1.097, 95% CI=1.043–1.154; P<0.001), KIM-1 (OR=1.736, 95% CI=1.290–2.338; P<0.001), and Podoplanin (OR=0.010, 95% CI=0.001–0.083; P<0.001) (Table 4). In addition, the multivariate logistic regression analysis results demonstrated that duration (OR=1.977, 95% CI=1.284–3.045; P=0.002), SBP (OR=1.089, 95% CI=1.035–1.145; P=0.001), Scr (OR=1.110, 95% CI=1.048–1.177; P<0.001), NGAL (OR=1.078, 95% CI=1.041–1.116; P<0.001), KIM-1 (OR=1.731, 95% CI=1.349–2.220; P<0.001), and Podoplanin (OR=0.022, 95% CI=0.005–0.100; P<0.001) (Table 5). Moreover, the ROC curve showed the optimal cutoff value of serum Podoplanin is 3.378 ng/mL (sensitivity: 81.4%; specificity: 77.3%; AUC = 0.853; Figure 3). The T2DM patients with low serum Podoplanin levels (<3.378 ng/mL) had a significantly higher risk of DN.

# Discussion

Our study investigated the impact of serum Podoplanin levels on diabetic nephropathy in patients with type 2 diabetes mellitus (T2DM). The findings revealed that serum Podoplanin levels were significantly lower in T2DM patients than in healthy individuals. Furthermore, the study observed a negative correlation between serum Podoplanin levels and factors

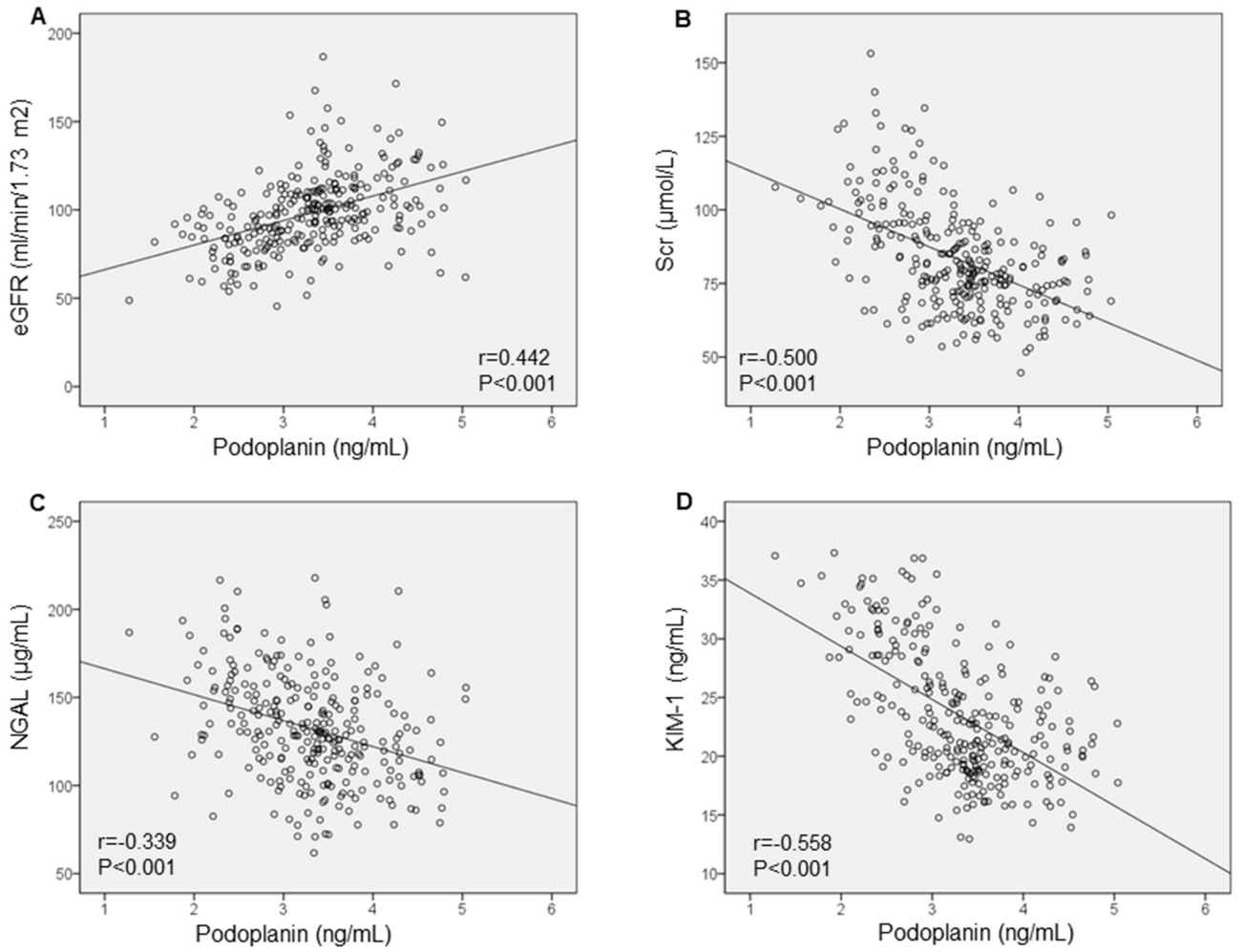


**Figure 2** The correlation between serum Podoplanin and clinical indicators. Pearson correlation test was performed between Podoplanin with (**A**) eGFR, (**B**) Scr, (**C**) NGAL and (**D**) KIM-1 in all T2DM patients.

such as age, BMI, duration of diabetes, SBP, DBP, FGP, HbA1c, TG, TC, LDL-C, Scr, NGAL, and KIM-1. On the other hand, HDL-C and eGFR showed a positive association with serum Podoplanin levels. Notably, T2DM patients with low serum Podoplanin levels (<3.378 ng/mL) were found to have a significantly higher risk of developing T2DM. Therefore, the results suggest that serum Podoplanin could serve as a potential biomarker for identifying the onset of diabetic nephropathy in patients with T2DM.

The concentration of Serum Podoplanin has been studied in individuals diagnosed with T2DM to understand its potential role in the progression of the disease and its associated complications. Podoplanin is a glycoprotein crucial in various physiological processes, such as lymphangiogenesis and platelet aggregation.[11] Research suggests that serum Podoplanin levels in T2DM patients may be linked to an increased risk of diabetes-related health issues.[14] This connection is due to Podoplanin's ability to influence the activities of endothelial cells, leading to vascular inflammation and the development of atherosclerosis, which are common complications in T2DM.[14] However, the present study showed that serum Podoplanin levels were lower in the T2DM patients (3.30±0.69 ng/mL) than in the healthy control groups (5.54±0.73 ng/mL).

Podoplanin, a glycoprotein extensively studied for its involvement in various clinical conditions,[15] is also gaining attention for its role in neurological disorders. Previous studies have shown that increased levels of podoplanin may indicate a higher risk of thrombus formation.[16] Some investigations suggest that elevated concentrations of podoplanin could be associated with poorer differentiation and a more unfavourable prognosis in lung carcinoma.[17] This diverse

**Table 4** Logistic Univariate Regression for Developing DN

| Characteristics | Odds Ratio | 95% CI | P-Value |
|---|---|---|---|
| Age (years) | 1.079 | 0.993–1.172 | 0.072 |
| Gender (male, %) | 1.657 | 0.366–7.513 | 0.513 |
| BMI (kg/m$^2$) | 1.109 | 0.482–2.553 | 0.807 |
| Duration (years) | 1.898 | 1.045–3.447 | 0.035 |
| SBP (mmHg) | 1.065 | 1.001–1.133 | 0.045 |
| DBP (mmHg) | 1.043 | 0.974–1.117 | 0.229 |
| FPG (mmol/L) | 1.208 | 0.500–2.919 | 0.675 |
| HbA1c (%) | 1.276 | 0.587–2.772 | 0.538 |
| TG (mmol/L) | 1.001 | 0.420–2.386 | 0.998 |
| TC (mmol/L) | 1.088 | 0.179–6.617 | 0.927 |
| LDL-C (mmol/L) | 3.450 | 0.235–50.655 | 0.366 |
| HDL-C (mmol/L) | 0.202 | 0.004–9.196 | 0.412 |
| eGFR (mL/min/1.73 m$^2$) | 0.973 | 0.934–1.015 | 0.203 |
| Scr (μmol/L) | 1.084 | 1.014–1.157 | 0.017 |
| NGAL (μg/mL) | 1.097 | 1.043–1.154 | <0.001 |
| KIM-1 (ng/mL) | 1.736 | 1.290–2.338 | <0.001 |
| Podoplanin (ng/mL) | 0.010 | 0.001–0.083 | <0.001 |

**Abbreviation**: CI, confidence interval.

**Table 5** Logistic Multivariate Regression for Developing DN

| Characteristics | Odds Ratio | 95% CI | P-Value |
|---|---|---|---|
| Duration (years) | 1.977 | 1.284–3.045 | 0.002 |
| SBP (mmHg) | 1.089 | 1.035–1.145 | 0.001 |
| Scr (μmol/L) | 1.110 | 1.048–1.177 | <0.001 |
| NGAL (μg/mL) | 1.078 | 1.041–1.116 | <0.001 |
| KIM-1 (ng/mL) | 1.731 | 1.349–2.220 | <0.001 |
| Podoplanin (ng/mL) | 0.022 | 0.005–0.100 | <0.001 |

function of podoplanin is further highlighted by growing research on its role in neurological disorders, such as ischemic stroke, where it may contribute to the pathophysiological mechanisms.[18] These findings suggest that serum podoplanin levels could be valuable indicators for multiple clinical conditions, particularly in assessing hypercoagulability, cancer prognosis, and immune status. In the current study, the correlation analysis between serum Podoplanin and clinical indicators showed that all 276 T2DM patients had negative associations with serum Podoplanin levels and age, BMI, duration, SBP, DBP, FPG, HbA1c, TG, TC, LDL-C, Scr, NGAL, and KIM-1, and a positive association with HDL-C and eGFR (Table 3). Using a Pearson correlation test, Podoplanin correlated with eGFR, Scr, NGAL, and KIM-1. The results indicated serum Podoplanin levels were negatively correlated with Scr, NGAL, and KIM-1, while eGFR positively correlated with Podoplanin levels (Figure 2).

The present investigation conducted univariate and multivariate logistic regression analyses to identify independent risk factors associated with DN. The findings from the univariate logistic regression analysis revealed that Scr (OR=1.084, 95% CI=1.014–1.157; P=0.017), NGAL (OR=1.097, 95% CI=1.043–1.154; P<0.001), KIM-1 (OR=1.736, 95% CI=1.290–2.338; P<0.001), and Podoplanin (OR=0.010, 95% CI=0.001–0.083; P<0.001) were statistically significant (Table 4). The multivariate logistic regression analysis further confirmed the importance of these factors, showing that duration of diabetes (OR=1.977, 95% CI=1.284–3.045; P=0.002), SBP (OR=1.089, 95% CI=1.035–1.145; P=0.001), Scr (OR=1.110, 95% CI=1.048–1.177; P<0.001), NGAL (OR=1.078, 95% CI=1.041–1.116; P<0.001), KIM-1 (OR=1.731, 95% CI=1.349–2.220; P<0.001), and Podoplanin (OR=0.022, 95% CI=0.005–0.100; P<0.001) were significant predictors (Table 5). The Receiver Operating Characteristic (ROC) curve analysis established that the optimal

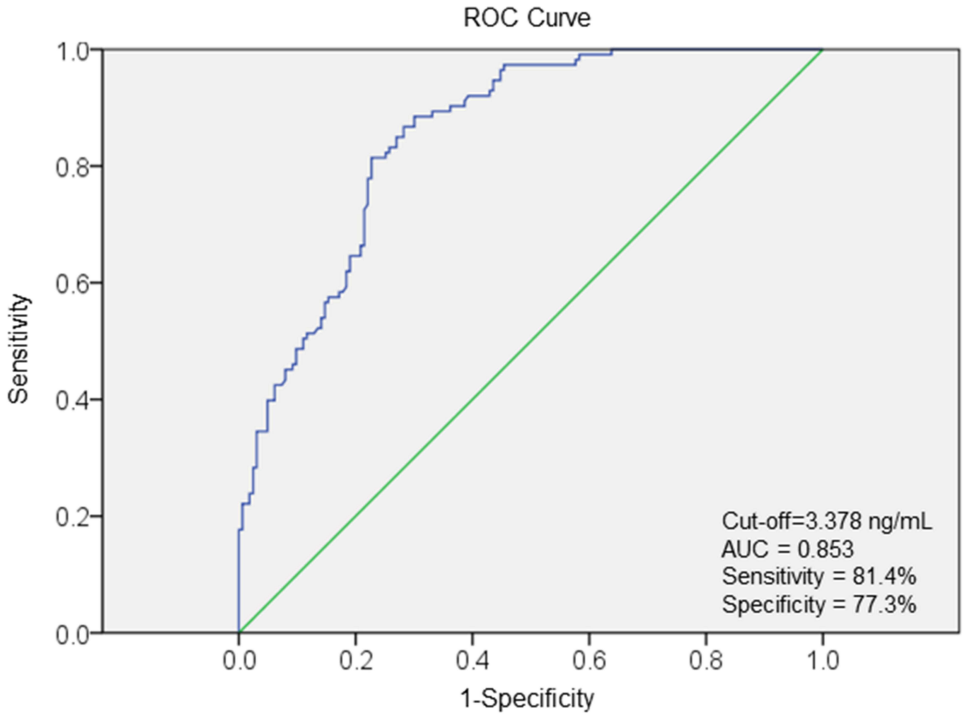


**Figure 3** The cut-off value of serum Podoplanin. The ROC curve was used to obtain the optimal cut-off value of serum Podoplanin (3378 ng/mL) that distinguishes the T2DM patients with and without albuminuria.

threshold for serum Podoplanin is 3.378 ng/mL, with a sensitivity of 81.4%, specificity of 77.3%, and an Area Under the Curve (AUC) of 0.853 (Figure 3). This research has practical implications, as it suggests that patients diagnosed with T2DM and low serum Podoplanin concentrations (<3.378 ng/mL) should be closely monitored due to their significantly higher risk of T2DM.

## Limitations

Several constraints are associated with our investigation. (1) Caution must be exercised in interpreting our findings due to the relatively limited size of our research cohort. (2) The nature of the study was not designed to be a prospective longitudinal investigation; instead, it was a cross-sectional design. The prognostic significance of serum Podoplanin necessitates further validation. (3) This research provides essential insights into the Podoplanin irregularities contributing to diabetic nephropathy dysfunction observed in patients with DN.

## Conclusions

The levels of serum Podoplanin are lower in diabetic patients with DN compared to healthy individuals. Lower levels of serum Podoplanin independently increase the risk of diabetic patients with DN. A more comprehensive population-based prospective study is needed to confirm the potential of serum Podoplanin as a predictor of diabetic patients with DN.

## Data Sharing Statement

The datasets used/analyzed during the present study are available from the corresponding author upon reasonable request.

## Ethics Approval and Consent to Participate

The Ethics Committee of Nantong Second People's Hospital approved this study. The authors followed all standard protocols in accordance with the 1964 Declaration of Helsinki. All subjects provided informed consent to participate in the study.

## Acknowledgment

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests.

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