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CORRELATION ANALYSIS OF SERUM CRK, CD138, AND APL WITH THE PROGNOSIS OF PATIENTS WITH DIABETIC NEPHROPATHY

KORELACIONA ANALIZA SERUMSKIH NIVOA CRK, CD138 I APL SA PROGNOZOM PACIJENATA SA DIJABETIČKOM NEFROPATIJOM

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Summary

Background: To explore the relationships between the levels of serum CITRON kinase-related kinase (CRK), syndecan-1 (CD138), and APJ receptor ligand (APL) and renal function and prognosis in patients with diabetic nephropathy.
Methods: From November 2023 to November 2025, 306 patients with diabetic nephropathy admitted to the hospital were selected as the study group, while 306 patients with simple diabetes were selected as the simple diabetes group; another 306 healthy individuals who underwent physical examinations during the same period composed the healthy control group. The levels of serum CRK, CD138, and APL were determined via enzyme-linked immunosorbent assay. Pearson correlation analysis was used to examine the relationships between serum CRK, CD138, and APL levels and clinical data in patients with diabetic nephropathy. To examine the variables determining a poor prognosis in patients with diabetic nephropathy, univariate and multivariate logistic regression analyses were performed. The prognostic value of serum CRK, CD138, and APL levels for unfavorable outcomes in individuals with diabetic nephropathy was examined using receiver operating characteristic (ROC) curves.
Results: Compared with those in the healthy control group, the levels of serum CRK and CD138 in patients in the simple diabetes group and the study group were increased, whereas the level of APL was decreased. The estimated glomerular filtration rate (eGFR) decreased in patients in the study group, and the urinary albumin-to-creatinine

Kratak sadržaj

Uvod: Cilj je bio da se ispita povezanost nivoa serumskog CITRON-kinaza srodnog enzima (CRK), sindekana-1 (CD138) i liganda APJ receptora (APL) sa bubrežnom funkcijom i prognozom kod pacijenata sa dijabetičkom nefropatijom.
Metode: U periodu od novembra 2023. do novembra 2025. godine, 306 pacijenata sa dijabetičkom nefropatijom primljenih u bolnicu je uključeno kao ispitivana grupa, dok je 306 pacijenata sa nekomplikovanim dijabetesom činilo grupu sa dijabetesom. Dodatnih 306 zdravih ispitanika koji su u istom periodu obavili sistematske preglede činilo je zdravu kontrolnu grupu. Nivoi CRK, CD138 i APL u serumu su određivani metodom enzimski vezanog imunosorbentnog testa (ELISA). Pirsonova korelaciona analiza je korišćena za ispitivanje povezanosti između nivoa CRK, CD138 i APL u serumu i kliničkih podataka kod pacijenata sa dijabetičkom nefropatijom. Radi identifikacije faktora koji određuju lošu prognozu sprovedene su univarijantna i multivarijantna logistička regresiona analiza. Prognostička vrednost serumskih nivoa CRK, CD138 i APL za nepovoljne ishode procenjena je pomoću ROC krivih.
Rezultati: U poređenju sa zdravom kontrolnom grupom, nivoi CRK i CD138 u serumu su bili povišeni kod pacijenata u grupi sa dijabetesom i u ispitivanoj grupi, dok je nivo APL bio snižen. Procijenjena brzina glomerularne filtracije (eGFR) je bila smanjena kod pacijenata u ispitivanoj grupi, dok je odnos albumina i kreatinina u urinu (UACR) bio povećan. Sve razlike su bile statistički značajne ($P<0,05$). Nivoi CRK, CD138, APL i UACR u serumu bili su viši u

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ratio (UACR) increased. All these differences were statistically significant (P<0.05). The levels of serum CRK, CD138, APL, and UACR in the study group were higher than those in the simple diabetes group, whereas eGFR was lower. All these differences were statistically significant (P<0.05). Pearson correlation analysis revealed that the levels of serum CRK, CD138, APL, and UACR in the study group were negatively correlated with eGFR (P<0.05) and positively correlated with renal disease stage, creatinine, 24-hour proteinuria, and UACR (P<0.05). Serum CRK, CD138, and APL levels, as well as the UACR, were higher (P<0.05) and the eGFR was lower (P<0.05) in the bad prognosis group than in the good prognosis group. Univariate and multivariate logistic regression analyses showed that serum CRK, CD138, and APL levels were associated with patients' prognosis (P<0.05). The results of the ROC curve analysis revealed that the combined area under the curve (AUC) of serum CRK, CD138, and APL for predicting poor prognosis was significantly greater than that of CRK (Z=2.857, P=0.007), CD138 (Z=2.429, P=0.018), and APL (Z=2.175, P=0.033).
Conclusion: The levels of CRK, CD138, and APL in the serum of patients with DN increase, and these increases are related to renal function. The combination of these three indicators has greater predictive efficacy for patient prognosis.

Keywords: diabetic nephropathy, CITRON kinase-related kinase, multiligand proteoglycan-1, APJ receptor ligand, renal function, prognostic analysis

ispitivanoj grupi nego u grupi sa dijabetesom, dok je eGFR bio niži (P<0,05). Pirsonova analiza je pokazala da su nivoi CRK, CD138, APL i UACR u serumu negativno korelisani sa eGFR (P<0,05), a pozitivno sa stadijumom bubrežne bolesti, nivoom kreatinina, 24-časovnom proteinurijom i UACR (P<0,05). U grupi sa lošom prognozom nivoi CRK, CD138, APL i UACR bili su viši (P<0,05), dok je eGFR bio niži (P<0,05) u poređenju sa grupom sa dobrom prognozom. Univarijantna i multivarijantna logistička regresiona analiza pokazale su da su nivoi CRK, CD138 i APL povezani sa prognozom pacijenata (P<0,05). Analiza ROC krivih je pokazala da je kombinovana površina ispod krive (AUC) za CRK, CD138 i APL u predviđanju loše prognoze značajno veća u odnosu na pojedinačne markere: CRK (Z=2,857, P=0,007), CD138 (Z=2,429, P=0,018) i APL (Z=2,175, P=0,033).
Zaključak: Nivoi CRK, CD138 i APL u serumu pacijenata sa dijabetičkom nefropatijom su povišeni i povezani sa bubrežnom funkcijom. Kombinovana primena ova tri pokazatelja ima veću prognostičku vrednost.

Ključne reči: dijabetička nefropatija, CITRON kinase-related kinase, multiligandni proteoglikan-1, ligand APJ receptora, bubrežna funkcija, prognostička analiza

Introduction

Diabetic nephropathy is one of the most common microvascular complications of diabetes. Its characteristics include marked glomerular filtration, glomerular sclerosis, and interstitial and tubular fibrosis. As the disease progresses, diabetic nephropathy may lead to renal insufficiency and eventually develop into end-stage renal disease. It poses a major risk to patients' health and well-being (1). According to statistics, in 2019, there were 443,000 cases of type 1 and type 2 diabetic nephropathy in China, with 76,000 deaths, and the total number of patients was 31.65 million, increasing annually (2). Therefore, early assessment of renal function and prognosis in patients with diabetic nephropathy is vital. In recent years, with the development of molecular biology technology, an increasing number of biomarkers related to diabetic nephropathy have been identified, which may provide references for early diagnosis, treatment, and prognostic assessment. Among them, Rho-associated coiled-coil-forming protein kinase 2 (CRK), multiligand proteoglycan-1 (CD138), and APJ receptor ligand (APL) have attracted attention for their roles in diabetic nephropathy. CRK is a nonreceptor protein kinase related to cytoskeleton remodeling (3). Elevated serum CRK levels are associated with idiopathic membranous nephropathy (4). CD138 is a cell-surface molecule involved in cell adhesion, migration, and signal transduction (5). The serum level of CD138 is elevated in children with nephrotic syndrome. APL is an endogenous vasoactive peptide with vasodilatory, anti-inflammatory, and antifibrotic functions (6–7). APL can reduce podocyte apoptosis in the kidney and alleviate diabetic nephropathy in mice (8–10). Currently, studies on CRK, CD138, and APL in patients with diabetic nephropathy are relatively rare, especially those examining their prognostic value.

Thus, the purpose of this study was to investigate the blood levels of CRK, CD138, and APL in individuals with diabetic nephropathy and to analyze their relationships with renal function and prognosis, providing new references for the treatment and prognostic assessment of diabetic nephropathy and thereby improving patient care.

Materials and Methods

General information

From November 2023 to November 2025, 306 patients with diabetic nephropathy were admitted to our hospital. With an average age of 57.57±10.01 years, the research group consisted of 102 females and 202 males. For the simple diabetes group, 306 individuals with simple diabetes during the same time period were chosen, with an average age of 57.22±10.23 years. Of these, 198

were male, and 108 were female. Within the same time period, 306 more healthy people with an average age of 57.89±10.36 years – 196 men and 110 women – were selected as the healthy control group. Age and sex differences across the three groups were not statistically significant ($P>0.05$).

Inclusion criteria: (1) diabetic nephropathy diagnosis conforms to the relevant standards of the guidelines; (2) simple diabetes diagnosis conforms to the relevant standards of the guidelines; and (3) complete clinical data.

Exclusion criteria: (1) Type 1 diabetes patients; (2) patients with polycystic kidney disease, nephrotic syndrome, stage 5 chronic kidney disease or end-stage renal disease who were receiving dialysis treatment; (3) patients with malignant tumors, autoimmune diseases, hematological diseases, or mental disorders; (4) patients using immunosuppressants, nephrotoxic drugs, etc., that may affect renal function and cause changes in serum indicators; and (5) patients with urinary tract infections, obstructions, etc., that may cause proteinuria.

The ethical committee at our hospital approved this study (approval number: HKYS-2026-A0285). Each participant completed the informed consent form and willingly participated in the study, as did their families.

Detection of serum CRK, CD138, and APL levels

On the day of admission, the patients in the study group and the simple diabetes group had 5 mL of blood drawn from the elbow vein in a fasting state. The blood was centrifuged to separate the supernatant, and the serum samples were stored at -80 °C for future use. CD138, APL, and serum CRK levels were measured by enzyme-linked immunosorbent assay. Professionals completed the detection process and strictly followed the instructions of the reagent kits. The CRK and APL detection kits were purchased from Shanghai Fursheng Industrial Co., Ltd. (item numbers A102810 and A099893). The CD138 detection kit was purchased from Shanghai Enlink Biotechnology Co., Ltd. (item number: ml105539).

Renal function indicator testing

On the day after admission, urine samples were collected from the healthy control group during the physical examination. Creatinine levels in urine and serum samples were measured by the picric acid method, and albumin levels in urine were measured by the immunoturbidimetric method. The formula for estimating the glomerular filtration rate (eGFR) is as follows: eGFR [mL/(min·1.73 m^2)] = 186 × serum creatinine concentration (mg/dL) - 1.154 × age - 0.203 (if female, multiply by 0.742). The following formula was used to determine the urine albumin-to-creatinine ratio (UACR): Albumin/creatinine in urine (UACR) (mg/g).

Prognostic assessment and follow-up

The patients in the study group were followed for 3 years through multiple channels, including outpatient visits and phone calls. The patients' conditions were recorded to determine whether they developed end-stage renal disease or died. Patients with an eGFR < 15 mL/(min·1.73 m^2) who had received dialysis or kidney transplantation treatment were classified as having an unfavorable prognosis and were included in the unfavorable prognosis group (n=62), whereas those without such conditions were classified as having a favorable prognosis and were included in the favorable prognosis group (n=244).

Data collection

Clinical data such as smoking history, drinking history, hypertension, hyperlipidemia, coronary heart disease, renal disease stage, and family history of diabetic nephropathy were collected. Patients in the study group had their fasting blood glucose, glycosylated hemoglobin, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol measured and compared.

Statistical analysis

The research data were statistically analyzed via SPSS 25.0. When P was less than 0.05, a difference was deemed statistically significant. One-way analysis of variance and the SNK-q test were used to compare many groups, while t tests were used to compare two groups. The measurement data are shown as $\bar{x}\pm s$ values. Comparisons between groups were performed using the χ^2 or corrected χ^2 test, and count data are presented as the number of instances (percentages) [n(%)]. Serum CRK, CD138, and APL levels were correlated with clinical data using Pearson's correlation. The stepwise forward method was used for a multivariate logistic analysis of the factors influencing poor prognosis in patients with diabetic nephropathy. The prognostic value of serum CRK, CD138, and APL levels for poor prognosis in individuals with diabetic nephropathy was examined using receiver operating characteristic (ROC) curves.

Results

Comparison of CRK, CD138, and APL levels and renal function indicators in the three groups of serum

Both the study group and the simple diabetes group had higher levels of CRK and CD138 than those in the healthy control group, whereas APL levels were lower.

The eGFR decreased, and the UACR increased; the differences were statistically significant ($P<0.05$).

The levels of CRK, CD138, and APL in the serum of the study group and the UACR were all higher than those in the simple diabetes group, the eGFR was lower than in the simple diabetes group, and the differences were statistically significant ($P<0.05$; see *Table I*).

Comparison of clinical data among different prognosis study groups

Serum CRK, CD138, and APL levels were higher in the poor prognosis group than in the good prognosis group, and the estimated glomerular filtration rate (eGFR) of renal function indicators was lower. The urine albumin-creatinine ratio (UACR) increased, and the proportions of patients with stage III and IV kidney disease, creatinine levels, and 24-hour proteinuria levels were greater. All the differences were statistically significant ($P<0.05$), see *Table II*.

Correlations between the serum levels of CRK, CD138, and APL and renal function indicators

According to the results of the Pearson correlation analysis, there was a negative association ($P<0.05$) between the study group's blood levels of CRK, CD138, and APL and the eGFRs of renal function markers and a positive correlation with renal disease stage, creatinine, 24-hour proteinuria, and the UACR ($P<0.05$), see *Table III*.

Logistic regression analysis of the factors influencing the prognosis of patients with diabetic nephropathy

The prognosis status of patients with diabetic nephropathy was used as the dependent variable (poor prognosis = 1, good prognosis = 0). The indicators with statistically significant differences in Table II (continuous variables were assigned their original values) were used as independent variables in a stepwise forward multivariate logistic regression analysis. As indicated in *Table IV*, the findings demonstrated that the prognosis of patients with diabetic nephropathy was influenced by the serum levels of CRK, CD138, and APL ($P<0.05$).

Predictive value of serum CRK, CD138, and APL levels for poor prognosis in patients with diabetic nephropathy

The test variables were serum CRK, CD138, and APL levels, and the dependent variable was the prognosis of patients with diabetic nephropathy (bad prognosis = 1; excellent prognosis = 0). Receiver operating characteristic (ROC) profiles were generated. When predicting a bad prognosis in patients with diabetic nephropathy, the serum CRK level's area under the curve (AUC) was 0.828, the CD138 level's AUC was 0.867, the APL level's AUC was 0.893, and the combined prediction of the three was 0.969. The combined prediction of the three was significantly greater than the predictions of CRK ($Z=2.857$, $P=0.007$), CD138 ($Z=2.429$, $P=0.018$), and APL ($Z=2.175$, $P=0.033$) alone (see *Table V*).

Table I Comparison of serum CRK, CD138, APL levels and renal function indicators among three groups ($\bar{x}\pm s$).

Group	n	CRK (μg/L)	CD138 (μg/L)	APL (μg/L)	EGFR [mL/(min ·1.73 m^2)]	UACR (mg/g)
Healthy control group	306	11.67±2.11	9.29±1.66	137.73±30.44	108.86±19.48	23.84±6.36
Simple diabetes group	306	14.34±2.98	12.47±2.52	63.74±15.61	105.97±19.29	24.65±6.13
Research group	306	24.29±4.90	17.15±3.10	83.90±18.42	75.48±17.43	109.85±43.47
F		532.105	369.598	443.660	149.236	570.835
P		<0.001	<0.001	<0.001	<0.001	<0.001

Table II Comparison of clinical data of patients in different prognostic study groups [n (%) or $\bar{x}\pm s$].

Item	Good prognosis group (n=244)	Poor prognosis group (n=62)	T/X2/Correction x^2	P
Gender			1.163	0.285
Male	156 (63.93)	46 (74.19)		
Female	88 (36.07)	16 (25.81)		
Age (years)	56.99±10.26	59.87±8.82	1.438	0.156
Course of diabetes (months)	94.18±22.81	108.65±23.41	1.618	0.101
Smoking history			0.509	0.470
Yes	78 (31.97)	24 (38.71)		
No	166 (68.03)	38 (61.29)		
Drinking history			0.367	0.549
Yes	88 (36.07)	26 (41.94)		
No	156 (63.93)	36 (58.06)		
Hypertension			2.701	0.103
Yes	52 (21.31)	22 (35.48)		
No	192 (78.69)	40 (64.52)		
Hyperlipidemia			0.632	0.427
Yes	16 (6.56)	8 (12.90)		
No	228 (93.44)	54 (87.10)		
Coronary heart disease			2.398	0.125
Yes	14 (5.74)	10 (16.13)		
No	230 (94.26)	52 (83.87)		
Family history of diabetes nephropathy			0.533	0.460
Yes	30 (12.30)	12 (19.35)		
No	214 (87.70)	50 (80.65)		
Staging of kidney disease			10.154	0.001
Phase I and II	156 (63.93)	20 (32.26)		
Phase III and IV	88 (36.06)	42 (67.74)		
C-reactive protein (mg/L)	9.49±2.77	10.54±2.81	1.889	0.064
Fasting blood glucose (mmol/L)	9.67±1.85	10.24±1.83	1.563	0.124
Glycated hemoglobin (%)	7.87±1.69	8.13±1.76	0.775	0.444
Total cholesterol (mmol/L)	5.23±1.13	5.38±1.15	0.679	0.503
Triacylglycerol (mmol/L)	1.99±0.37	2.09±0.38	1.481	0.132
High-density lipoprotein cholesterol (mmol/L)	1.19±0.28	1.17±0.25	0.400	0.688
Low density lipoprotein cholesterol (mmol/L)	2.89±0.55	3.07±0.69	1.628	0.109
Creatinine (μmol/L)	172.64±40.29	216.75±35.00	5.586	<0.001
24-hour proteinuria (mg/24 h)	613.14±155.09	789.95±186.93	5.433	<0.001
CRK (μg/L)	22.63±4.45	30.72±5.91	8.538	<0.001
CD138 (μg/L)	15.97±3.04	21.79±4.19	8.840	<0.001
APL (μg/L)	76.94±16.81	111.77±20.73	9.784	<0.001
EGFR [mL/(min ·1.73 m^2)]	79.18±14.56	60.81±11.70	6.975	<0.001
UACR (mg/g)	102.12±22.11	139.87±25.97	8.140	<0.001

Table III Correlation analysis between serum CRK, CD138, APL levels, and renal function indicators

Indicator	CRK		CD138		APL	
	r	P	r	P	r	P
Staging of kidney disease	0.579	<0.001	0.597	<0.001	0.592	<0.001
Creatinine	0.549	<0.001	0.555	<0.001	0.563	<0.001
24-hour proteinuria	0.536	<0.001	0.531	<0.001	0.548	<0.001
EGFR	-0.578	<0.001	-0.551	<0.001	-0.536	<0.001
UACR	0.680	<0.001	0.674	<0.001	0.653	<0.001

Table IV Logistic regression analysis of adverse factors in patients with diabetes nephropathy.

Item	Univariate analysis				Multivariate analysis			
	SE	OR	95% CI	P	SE	OR	95% CI	P
CRK	0.302	2.295	1.254~4.203	0.001	0.311	2.488	1.335~4.638	<0.001
CD138	0.266	1.939	1.159~3.245	0.015	0.244	1.889	2.087~3.028	<0.001
APL	0.270	2.093	1.217~3.590	0.001	0.263	2.193	1.319~3.649	<0.001

Table V Predictive value of serum CRK, CD138, and APL levels for poor prognosis of patients with diabetes nephropathy.

Item	AUC	Cutoff value	Sensitivity (%)	Specificity (%)	95%CI	Youden index
CRK	0.828	24.977 μg/L	87.13	68.93	0.739~0.917	0.563
CD138	0.867	18.318 μg/L	83.93	80.33	0.781~0.932	0.645
APL	0.893	95.718 μg/L	74.23	88.53	0.835~0.941	0.620
Joint efforts of the three parties	0.969	-	87.13	97.53	0.934~1.003	0.849

Discussion

Diabetic nephropathy is a common complication of diabetes. The assessment of the prognosis of this condition is highly important for long-term health and disease management. Research on biomarkers has shown that serum markers such as CRK, CD138, and APL can reflect the extent of damage in diabetic nephropathy and are associated with patients' renal function (11). Some markers related to renal injury are also associated with patient prognosis (12). Therefore, additional biomarkers related to patient prognosis are needed to accurately assess disease progression risk and formulate individualized treatment plans to delay progression and improve patient outcomes.

CRK is a serine/threonine protein kinase downstream of the small G protein of the Rho kinase family, which affects various functions, such as cell contraction, migration, adhesion, and proliferation. In a cell model of diabetic nephropathy, high CRK expression promoted cell proliferation and fibrosis and accelerated disease progression (13). In this study, the serum CRK level in patients with diabetic nephropathy was elevated, and this elevation was associated with renal function, suggesting that CRK is involved in the development of diabetic nephropathy. CRK may inhibit peroxisome proliferator-activated receptors, modulate the nodes of energy homeostasis, regulate the transcription of fatty acid oxidation-related genes, and induce podocyte apoptosis in diabetic nephropathy (14). In addition, CRK is closely associated with increased levels of profibrotic factors, leading to albuminuria, glomerular sclerosis, and podocyte damage (15). CRK may affect the proliferation of renal tubular epithelial cells through the PI3K/AKT pathway, promote

apoptosis and epithelial-mesenchymal transition, and thereby regulate the onset and progression of diabetic nephropathy (16).

CD138 is a type I transmembrane glycoprotein of the heparan sulfate proteoglycan family, involved in processes such as cell differentiation, adhesion, diffusion, migration, and cytoskeletal organization. It is closely related to vascular endothelial permeability. The serum CD138 level in patients with type 2 diabetes is higher than that in nondiabetic patients. It is closely associated with proteinuria (17). In this study, the serum CD138 levels of patients with diabetic nephropathy were elevated and correlated with renal function, suggesting that abnormal CD138 levels may contribute to renal dysfunction in diabetic nephropathy. A possible reason is that CD138 is a surface protein on epithelial cells that participates in processes such as maintaining cell morphology and polarity. In diabetic nephropathy, a high-sugar environment may promote cell polarity loss and apoptosis, thereby elevating serum CD138 levels (18). CD138 may promote the production of extracellular matrix by renal tubular epithelial cells, thereby promoting the differentiation of fibroblast-like cells and the occurrence of renal fibrosis (19). In addition, CD138 expression may be regulated by the mTOR signaling pathway, and mTOR signaling pathway activation is closely associated with inflammation in renal endothelial cells (20).

APL is a bioactive polypeptide belonging to the apelin family. It is a fat cell factor derived from a 77-amino-acid precursor protein through posttranslational processing and cleavage at enzymatic sites. It plays important roles in regulating the cardiovascular system, myocardial infarction repair, anti-atherosclerosis, and neuroprotection, among other functions (21). In this study, the serum APL level in patients with diabetic nephropathy was higher than that in patients with simple diabetes, was closely related to renal function, but was significantly lower than that in healthy controls, suggesting that abnormal APL is associated with renal injury and is involved in the occurrence and development of diabetic nephropathy. The possible reason is that APL reduces renal tissue fibrosis by increasing nitric oxide production, alleviating the progression of diabetic nephropathy (22); however, since the kidneys are the main organ for clearing APL, when renal function decreases, the clearance rate decreases, increasing the serum APL level in patients with kidney disease (23).

Serum CRK, CD138, and APL levels in the research group were found to be negatively correlated with the estimated glomerular filtration rate (eGFR) of renal function indicators and positively correlated with creatinine, 24-hour proteinuria, kidney disease stages, and urinary albumin-creatinine ratio (UACR) indicators, according to the study's Pearson correlation analysis. These findings suggest that these three factors may be involved in the occurrence and progression of the disease by influencing renal function. Additionally, the results of univariate and multivariate logistic analyses indicated that Diabetic nephropathy patients' poor prognosis was influenced by serum CRK, CD138, and APL levels. These results imply that these three variables may be crucial for determining the prognosis of diabetic nephropathy and for identifying high-risk individuals, enabling early development of intervention and treatment plans.

Conclusion

Serum levels of CRK, CD138, and APL were elevated in patients with diabetic nephropathy and were closely associated with renal function. Using these three parameters together yielded a comparatively high predictive efficacy for patient prognosis. However, this study is subject to certain restrictions, namely a limited sample size, which could compromise the accuracy and applicability of the findings. Future studies should be conducted with larger samples and in multicenter settings to verify. Additionally, the specific mechanisms by which APL, CD138, and CRK affect renal function and diabetic nephropathy remain to be further explored.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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