

Cite as: Fu XZ, Li YX, Liu CF, Wang YG. Effectiveness and safety of *Jinhu Gushen* Formula in diabetic kidney disease patients with massive proteinuria: a retrospective cohort study [J]. Chin J Clin Res, 2025, 38(9):1342-1345,1349.

DOI: 10.13429/j.cnki.cjcr.2025.09.009

Effectiveness and safety of *Jinhu Gushen* Formula in diabetic kidney disease patients with massive proteinuria: a retrospective cohort study

FU Xinzhi*, LI Yixuan, LIU Chuanfeng, WANG Yangang

*Department of Endocrinology, The Affiliated Hospital of Qingdao University, Qingdao, Shandong 266003, China

Corresponding author: WANG Yangang, E-mail: wangyg1966@126.com

Abstract: Objective To evaluate the effect of *Jinhu Gushen* Formula on renal function in diabetic kidney disease (DKD) patients with massive proteinuria and to evaluate its efficacy and safety. **Methods** A retrospective cohort study was conducted on 88 DKD patients with massive proteinuria admitted to the Department of Endocrinology, the Affiliated Hospital of Qingdao University from June 2023 to June 2025. According to the treatment plan, the patients were divided into the *Jinhu Gushen* Formula group ($n=43$) and the finerenone group ($n=45$). Renal function indicators [urine albumin- to-creatinine ratio (UACR), serum creatinine, serum uric acid, estimated glomerular filtration rate (eGFR)] and safety indicators (serum potassium) between two groups of patients were compared. Results For patients with massive proteinuria, the *Jinhu Gushen* Formula group demonstrated a lightly higher effective rate compared to the finerenone group without significant statistical significance [88.37% (38/43) vs 77.78% (35/45), $\chi^2=1.745$, $P=0.186$]. The serum uric acid level in the *Jinhu Gushen* Formula group was significantly lower than that in the finerenone group [$(340.51 \pm 87.06) \mu\text{mol/L}$ vs $(383.96 \pm 90.04) \mu\text{mol/L}$, $t=2.301$, $P=0.024$], and the rate of uric acid reduction was significantly greater in the *Jinhu Gushen* Formula group ($4.88\% \pm 24.98\%$ vs $-9.66\% \pm 25.09\%$, $t=2.724$, $P=0.008$). In terms of safety, the serum potassium level in the *Jinhu Gushen* Formula group was significantly lower than that in the finerenone group [$(4.59 \pm 0.34) \text{mmol/L}$ vs $(4.94 \pm 0.47) \text{mmol/L}$, $t=2.719$, $P=0.010$], with a significantly lower rate of potassium elevation observed in the *Jinhu Gushen* Formula group ($-0.22\% \pm 8.34\%$ vs $9.23\% \pm 8.60\%$, $t=3.529$, $P=0.001$). **Conclusion** *Jinhu Gushen* Formula has a similar effect as finerenone in reducing UACR in DKD patients, and can better reduce blood uric acid levels in DKD patients, with good safety.

Keywords: Diabetic kidney disease; *Jinhu Gushen* Formula; Proteinuria; Serum uric acid; Serum potassium; Finerenone

Fund program: National Science and Technology Major Project (2024ZD0523505)

In recent years, with the global rise in the prevalence of diabetes, diabetic kidney disease (DKD), an important microvascular complication of diabetes, has significantly increased the global disease burden [1]. By 2025, nearly one-third of diabetic patients in China will have DKD [2]. The onset of DKD has a profound impact on the long-term prognosis and quality of life of diabetic patients. Currently, the clinical treatment of DKD mainly relies on blood glucose management, blood pressure control, and proteinuria reduction [3-4]. Non-steroidal mineralocorticoid receptor antagonists (ns-MRAs), such as finerenone, are currently the only drugs that reduce proteinuria in DKD patients and play a key role in both monotherapy and combination therapy. In recent years, Chinese medicine has gained prominence in the treatment of DKD and has gradually become an important therapeutic approach. This shift is attributed to Chinese medicine's multi-target effects in the treatment process, which align with the progression of DKD, leveraging its individualized and dynamic intervention characteristics. These effects collectively regulate the genetic, oxidative metabolism, and inflammatory responses of kidney cells [5]. The *Jinhu Gushen* Formula, developed by Professor WANG Yanggang from the Affiliated Hospital of Qingdao University for the treatment of DKD, has the effects of "tonifying Yang and solidifying the kidneys, benefiting Qi and nourishing Yin, strengthening the spleen, and resolving blood stasis". This study aims to compare the efficacy of *Jinhu Gushen* Formula and finerenone in reducing urine protein levels and improving kidney

function in DKD patients, with the goal of promoting the application of Chinese medicine in the treatment of DKD and providing new therapeutic options for clinical treatment of DKD patients.

1 Subjects and Methods

1.1 Study Subjects and Grouping

This cohort study retrospectively selected 88 DKD patients who visited the Outpatient Endocrinology Department of the Affiliated Hospital of Qingdao University from June 2023 to June 2025. The patients were divided into two groups based on the medication used for proteinuria reduction: the *Jinhu Gushen* Formula group (*Jinhu Gushen* Formula + basic DKD treatment) and the finerenone group (finerenone + basic DKD treatment). This study has been approved by the Ethics Committee of the Affiliated Hospital of Qingdao University (Ethics No.: QYFY WZLL30229).

1.2 Inclusion Criteria

(1) Age ≥ 18 years, body mass index (BMI) $\leq 45 \text{ kg/m}^2$;
(2) Diagnosis of DKD with heavy proteinuria according to the *Chinese Diabetes Kidney Disease Prevention and Treatment Guidelines (2021 Edition)* [6] and the *Expert Consensus on the Integrated Prevention and Treatment of Diabetic Kidney Disease with Traditional Chinese and Western Medicine (2023 Edition)* [7]; (3) Diabetes duration

≥ 5 years;(4) Historical data ≥ 3 months, with complete medical records.

1.3 Exclusion Criteria

(1) Recent history of acute diabetic complication (hypoglycemic coma, diabetic ketoacidosis, lactic acidosis, etc.); (2) Presence of other diseases that may affect kidney function or urine protein excretion (such as heart failure, myocardial infarction, infections, autoimmune diseases, etc.), or other malignancies (e.g., malignant tumors); (3) Initial urine albumin-to-creatinine ratio (UACR) <30 mg/g; (4) Need for dialysis or kidney transplant; (5) Un-standard treatment that may affect efficacy assessment.

1.4 Treatment Protocol

1.4.1 Jinhu Gushen Formula Group

The treatment protocol involved Jinhu Gushen Formula + basic DKD therapy. The Jinhu Gushen Formula consists of Huangqi (*Astragali Radix*, 黄芪), Fuchao Baizhu (*Atractylodis Macrocephalae Rhizoma*, 麸炒白术), Jinyingzi (*Rosae Laecigatae Fructus*, 金樱子), Ciwujia (*Acanthopanax Senticosi Radix Et Rhizome Seu Caulis*, 刺五加), Jixuecao (*Centellae Herba*, 积雪草), Danshen (*Salviae Miltiorrhizae Radix Et Rhizoma*, 丹参), Gegen (*Puerariae Lobatae Radix*, 葛根), Chuanniuxi (*Cyathulae Radix*, 川牛膝), Nvzhenzi (*Ligustri Lucidi Fructus*, 女贞子), Huluba (*Trigonellae Semen*, 胡芦巴), Guizhi (*Cinnamomi Ramulus*, 桂枝), Banzhilian (*Scutellariae Barbatae Herba*, 半枝莲), Fubaishao (*Paeoniae Radix Alba*, 麸白芍), Yanduzhong (*Eucommiae Cortex*, 盐杜仲), Sanqi powder (*Notoginseng Radix Et Rhizoma*, 三七粉). The treatment dosage was 250 mL twice daily, taken after meals, for a continuous period of 3 months.

1.4.2 Finerenone Group

The treatment protocol involved finerenone + basic DKD therapy. Finerenone tablets (Bayer Pharmaceuticals, batch number: HJ20220058, 20 mg/tablet) were given at a dosage of 1 tablet once daily, continuously for 3 months. During the treatment period, the blood glucose, blood pressure, and lipid-lowering regimens remained unchanged, following the prescribed dosages and frequencies as per the product instructions (no medication exceeded the recommended dosages; insulin maintenance dosage fluctuation was under 10%).

1.5 Observational Indicators

1.5.1 General Data

General data included: age, gender, diabetes duration, BMI, pre-treatment UACR, estimated glomerular filtration rate (eGFR), blood potassium, blood creatinine, blood uric acid, fasting blood glucose (FBG), blood lipids [triglycerides (TG), low-density lipoprotein (LDL)], glycated hemoglobin (HbA_{1c}), and medication regimens.

1.5.2 Efficacy and Safety Indicators

Primary efficacy indicators included UACR, serum creatinine, and serum uric acid. Secondary efficacy

indicators included eGFR. The safety indicator was blood potassium levels.

1.5.3 Clinical Efficacy Indicators

(1) UACR reduction rate;(2) Treatment efficacy rate (treatment was considered effective if UACR decreased to the normal range or decreased by more than 30% from baseline); (3) Treatment effectiveness level: the proportion of patients classified as effective, significantly effective, or ineffective (treatment was considered effective if UACR reduction 30%~<50%, significantly effective if it was ≥ 50%, and ineffective in all other cases) [8].

1.6 Statistical Methods

All data in this study were analyzed using R4.5.0 software. For normally distributed continuous variables, data were expressed as $\bar{x} \pm s$, and intergroup comparisons were performed using the *t*-test. For non-normally distributed continuous variables, data were expressed as *M*(*P*₂₅,*P*₇₅), and comparisons were made using the Wilcoxon rank-sum test. Categorical data were expressed as cases (%), and intergroup comparisons were performed using the Chi-square test. For ordered categorical data, rank-sum tests were used. A *P*-value of <0.05 was considered statistically significant.

2 Results

2.1 General Data Analysis of the Two Groups

A total of 88 patients were included in this study. The Jinhu Gushen Formula group had 43 patients, and the finerenone group had 45 patients. There was no significant difference between the two groups in terms of age, gender, duration of diabetes, BMI, FBG, HbA_{1c}, TG, LDL, and medication regimens (*P*<0.05). See Table 1.

Tab. 1 Comparison of general data between two groups

Indicators	Jinhu Gushen Formula group (n=43)	Finerenone group (n=45)	t/χ ² value	P value
Age(year) ^a	60.93±13.19	62.18±12.37	0.457	0.649
Male ^b	30(69.77)	29(64.44)	0.093	0.761
Diabetes duration (year) ^a	16.3±10.46	15.82±8.15	0.239	0.812
BMI(kg/m2) ^a	25.48±3.83	25.47±3.19	0.012	0.991
Biochemical parameters				
FBG(mmol/L) ^a	7.29±1.92	6.93±1.92	0.890	0.376
HbA1C(%) ^a	7.77±1.57	7.49±1.34	0.922	0.359
TG(mmol/L) ^a	1.43±0.72	1.46±0.65	0.179	0.858
LDL(mmol/L) ^a	2.71±0.82	2.52±1.02	0.938	0.351
Hypoglycemic drugs				
GLP-1RA ^b	6(13.95)	11(24.44)	0.953	0.329
Insulin ^b	23(53.49)	22(48.89)	0.048	0.827
Metformin ^b	14(32.56)	17(37.78)	0.084	0.772
α-glucosidase inhibitor ^b	7(16.28)	12(26.67)	0.855	0.355
DPP-4i ^b	20(46.51)	24(53.33)	0.182	0.670
TZD ^b	7(16.28)	4(8.89)	0.526	0.468
SGLT-2i ^b	27(62.79)	30(66.67)	0.025	0.875
Sulfonylureas ^b	8(18.60)	5(11.11)	0.476	0.490
antihypertensive drugs				
ACEI/ARB ^b	25(58.14)	21(48.89)	0.430	0.512
CCB ^b	18(41.86)	22(48.89)	0.200	0.654
Diuretic ^b	8(18.60)	4(8.89)	1.034	0.309
Lipid regulating agent				
Statins ^b	19(44.19)	22(48.89)	0.052	0.819
Fibrates ^b	4(9.30)	1(2.22)	0.948	0.330
Other kidney preserving drugs ^b	19(44.19)	22(48.89)	0.052	0.819

Note: a meant the data was represented by the form of $\bar{x} \pm s$; b meant the data was represented by the form of case(%).

2.2 Comparison of Therapeutic Efficacy Between the Two Groups

In patients with heavy proteinuria (UACR ≥ 300 mg/g), the treatment efficacy of the *Jinhu Gushen* Formula group was similar to that of the finerenone group [88.37% (38/43) vs 77.78% (35/45), $\chi^2=1.745$, $P=0.186$]. The comparison of the treatment effectiveness between the two groups is shown in **Table 2**. After treatment, the serum uric acid level in the *Jinhu Gushen* Formula group was significantly lower than that in the finerenone group ($P<0.05$). The decrease rate of serum uric acid in the *Jinhu Gushen* Formula group was significantly higher than that in the finerenone group ($4.88\% \pm 24.98\%$ vs $-9.66\% \pm 25.09\%$, $t=2.724$, $P=0.008$), but there was no significant difference in the decrease rate of UACR ($51.68\% \pm 16.20\%$ vs $46.18\% \pm 18.28\%$, $t=1.496$, $P=0.138$), serum creatinine ($2.81\% \pm 14.18\%$ vs $1.28\% \pm 15.19\%$, $t=0.491$, $P=0.625$), and the increase rate of eGFR ($1.93\% \pm 9.18\%$ vs $-3.95\% \pm 10.75\%$, $t=1.859$, $P=0.071$). The comparison of kidney function before and after treatment is shown in **Table 3**.

Tab.3 Comparison of renal function indicators before and after treatment between the *Jinhu Gushen* Formula group and the finerenone group ($\bar{X} \pm s$),

Group	<i>Jinhu Gushen</i> Formula group(n=43)	Finerenone group(n=45)	Z/t value	P value
UACR	Pre-treatment	916.24(490.15,1 453.64)	7.379	0.787
	Post-treatment	337.88(237.78,693.33)	6.832	0.728
SUA	Pre-treatment	376.77 $\pm$ 113.49	0.563	0.575
	Post-treatment	340.51 $\pm$ 87.06	2.301	0.024
SCr	Pre-treatment	340.51 $\pm$ 87.06	0.323	0.748
	Post-treatment	80.00 $\pm$ 27.78	0.454	0.651
eGFR	Pre-treatment	86.48 $\pm$ 16.94	0.994	0.326
	Post-treatment	88.31 $\pm$ 19.25	1.656	0.106

3 Discussion

Although many medications have been confirmed to delay the progression of DKD in recent years [9], some patients still experience continuous deterioration of kidney function, necessitating the development of new drugs for more effective treatment [5]. Chinese medicine has shown great potential in the recent treatment of DKD. After years of hyperglycemia, dyslipidemia, and hypertension, diabetic patients undergo degeneration of renal tissue. *Jinhu Gushen* Formula is a fixed prescription developed under the guidance of Chinese medicine theory, focusing on tonifying Yang and consolidating the kidneys, refined through years of clinical practice. Author team’s earlier study compared the clinical efficacy of *Jinhu Gushen* Formula and *Huangkui* capsules and confirmed the improvement in kidney function in DKD patients treated with *Jinhu Gushen* Formula [10]. This study further utilized a retrospective cohort study to compare *Jinhu Gushen* Formula with finerenone, aiming to assess its efficacy and safety in the treatment of DKD.

As a new generation of ns-MRAs, finerenone has been explored in two phase III clinical trials [11-12]. It is currently recommended in multiple national guidelines as an excellent treatment for delaying DKD progression [6-7,13]. UACR has become a key indicator for assessing the treatment effects of medications for chronic kidney disease in recent years [14-16]. The results of this study showed

2.3 Safety Comparison Between the Two Groups

Before treatment, there was no significant difference in serum potassium levels between the *Jinhu Gushen* Formula group and the finerenone group [(4.62 $\pm$ 0.43) mmol/L vs (4.54 $\pm$ 0.43) mmol/L, $t=0.599$, $P=0.553$]. After treatment, the serum potassium level in the *Jinhu Gushen* Formula group was significantly lower than that in the finerenone group [(4.59 $\pm$ 0.34) mmol/L vs (4.94 $\pm$ 0.47) mmol/L, $t=2.719$, $P=0.010$]. The increase rate of serum potassium in the *Jinhu Gushen* Formula group was significantly lower than that in the finerenone group ($-0.22\% \pm 8.34\%$ vs $9.23\% \pm 8.60\%$, $t=3.529$, $P=0.001$).

Tab.2 Comparison of the effectiveness of two treatment groups

Group	Significantly effective	Effective	Invalid
<i>Jinhu Gushen</i> Formula group(n=43)	22(51.16)	16(37.21)	5(11.63)
finerenone group(n=45)	18(40.00)	17(37.78)	10(22.22)
Z value		1.319	
P value		0.103	

that the treatment efficacy of the *Jinhu Gushen* Formula group was higher than that of the finerenone group (88.37% vs 77.78%), but the difference was not statistically significant, possibly due to the small sample size of this study. Nevertheless, this study indicates that the treatment with *Jinhu Gushen* Formula in patients with heavy proteinuria in DKD achieves a UACR-lowering effect similar to that of finerenone. Moreover, research has pointed out that lowering serum uric acid helps delay the progression of DKD and improve long-term patient prognosis [17]. Therefore, serum uric acid was selected as one of the primary outcome indicators in this study. The comparison between the groups showed a statistically significant difference in serum uric acid changes. In patients with heavy proteinuria in DKD, treatment with *Jinhu Gushen* Formula led to a general downward trend in serum uric acid, and the decrease rate of serum uric acid in the *Jinhu Gushen* Formula group was significantly higher than that in the finerenone group, indicating better control of serum uric acid. The incidence of hyperkalemia-related adverse events is higher with finerenone [12,18], limiting its clinical application. In this study, patients treated with *Jinhu Gushen* Formula maintained safe serum potassium levels during the 3-month follow-up, with a lower incidence of serum potassium increase compared to those treated with finerenone. In summary, *Jinhu Gushen* Formula shows similar effects to finerenone in improving kidney function and offers a unique advantage in

stabilizing serum potassium levels and improving the hyperuricemia status in DKD patients. This could potentially apply to a broader patient population, providing a new clinical treatment option for DKD patients with heavy proteinuria.

Recent studies have shown that increased proteinuria and kidney function decline in DKD patients are closely related to podocyte apoptosis, dysfunction, and inflammatory thickening of the glomerular basement membrane [19-20]. Current basic research shows that the main ingredients in *Jinhu Gushen* Formula, Jinyingzi and Huluba, exhibit strong antioxidant and anti-inflammatory activities [21-22]. Together, they protect the kidneys through multiple pathways, such as inhibiting the p38 MAPK/NF- κ B signaling pathway [23], regulating tryptophan metabolism [24], modulating the PI3K/AKT/ERK signaling pathway, and lipid metabolism [21].

This study has some limitations. First, the follow-up period was short, and the early efficacy of *Jinhu Gushen* Formula in improving long-term prognosis requires further exploration. Additionally, this study is a single-center retrospective study with limited generalizability. Future multi-center, large-sample prospective studies are needed to further validate the conclusions of this study and promote the clinical application of *Jinhu Gushen* Formula in DKD treatment.

In conclusion, based on the results of this study, *Jinhu Gushen* Formula demonstrates similar UACR-lowering effects to finerenone, while also reducing serum uric acid levels, having a lower incidence of hyperkalemia, and showing good safety.

Conflict of Interest None

References

- [1] Fenta ET, Eshetu HB, Kebede N, et al. Prevalence and predictors of chronic kidney disease among type 2 diabetic patients worldwide, systematic review and meta-analysis[J]. *Diabetol Metab Syndr*, 2023, 15(1): 245.
- [2] Jia WP, Yu R, Wang LM, et al. Prevalence of chronic kidney disease among Chinese adults with diabetes: a nationwide population-based cross-sectional study[J]. *Lancet Reg Health West Pac*, 2025, 55: 101463.
- [3] Naaman SC, Bakris GL. Diabetic nephropathy: update on pillars of therapy slowing progression[J]. *Diabetes Care*, 2023, 46(9): 1574-1586.
- [4] Zhao MM, Cao YT, Ma L. New insights in the treatment of DKD: recent advances and future prospects[J]. *BMC Nephrol*, 2025, 26(1): 72.
- [5] Cai RS, Li CY, Zhao Y, et al. Traditional Chinese medicine in diabetic kidney disease: multifaceted therapeutic mechanisms and research progress[J]. *Chin Med*, 2025, 20(1): 95.
- [6] Xue YM, Zhu DL. Clinical guideline for the prevention and treatment of diabetic kidney disease in China (2021 edition)[J]. *Chin J Diabetes Mellit*, 2021, 13(8).
- [7] The Diabetic Kidney Disease Group of Endocrine Committee of Chinese Association of Integrative Medicine, Chinese Medicine and Microcirculation Committee of the Chinese Society of Microcirculation. Expert consensus on the prevention and treatment of diabetic kidney disease with the integrated traditional Chinese and Western medicine (2023 edition) [J]. *Chin J Diabetes Mellitus*, 2023, 15(8): 690-702. [In Chinese]
- [8] Mentz RJ, Anker SD, Pitt B, et al. Efficacy and safety of finerenone in patients with chronic kidney disease and type 2 diabetes by diuretic use: a FIDELITY analysis[J]. *Eur J Heart Fail*, 2025, 27(5): 764-774.
- [9] Yamazaki T, Mimura I, Tanaka T, et al. Treatment of diabetic kidney disease: current and future[J]. *Diabetes Metab J*, 2021, 45(1): 11-26.
- [10] Li YX, Huang YJ, Wei FX, et al. Clinical effect of *Jinhu Gushen* prescription in reducing urinary protein and blood uric acid in patients with diabetic kidney disease[J]. *J Precis Med*, 2025, 40(2): 102-107. [In Chinese]
- [11] Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes[J]. *N Engl J Med*, 2021, 385(24): 2252-2263.
- [12] Bakris GL, Agarwal R, Anker SD, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes[J]. *N Engl J Med*, 2020, 383(23): 2219-2229.
- [13] ElSayed NA, McCoy RG, Aleppo G, et al. 11. chronic kidney disease and risk management: standards of care in diabetes—2025[J]. *Diabetes Care*, 2025, 48(Supplement 1): S239-S251.
- [14] Liu D, Lv LL. New understanding on the role of proteinuria in progression of chronic kidney disease[M]//*Renal Fibrosis: Mechanisms and Therapies*. Singapore: Springer Singapore, 2019, 1165: 487-500.
- [15] Yang F, Shao XJ, Huo YY, et al. Relationship between serum bilirubin and UACR in patients with diabetic foot ulcer[J]. *J Trop Med*, 2024, 24(9): 1283-1288. [In Chinese]
- [16] Chen JY, Xu XR, Zai GT, et al. Relationship between plasma low-density lipoprotein subtypes and diabetic nephropathy in T2DM patients[J]. *Chin J Clin Res*, 2023, 36(3): 445-449. [In Chinese]
- [17] Mauer M, Doria A. Uric acid and risk of diabetic kidney disease[J]. *J Nephrol*, 2020, 33(5): 995-999.
- [18] Agarwal R, Filippatos G, Pitt B, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis[J]. *Eur Heart J*, 2022, 43(6): 474-484.
- [19] Mohandes S, Doke T, Hu HL, et al. Molecular pathways that drive diabetic kidney disease[J]. *J Clin Invest*, 2023, 133(4): e165654.
- [20] Antar SA, Ashour NA, Sharaky M, et al. Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments[J]. *Biomed Pharmacother*, 2023, 168: 115734.
- [21] Niu Y, Niu HJ, Chi LX, et al. *Trigonella foenum-graecum* L. protects against renal function decline in a mouse model of type 2 diabetic nephropathy by modulating the PI3K-Akt-ERK signaling pathway[J]. *Front Pharmacol*, 2025, 16: 1566723.
- [22] Chen S, Wang L, Rong S, et al. Extraction, purification, chemical characterization, and in vitro hypoglycemic activity of polysaccharides derived from *Rosa laevigata* Michx[J]. *Int J Biol Macromol*, 2024, 279(Pt 1): 135116.
- [23] Wu HT, Lin TT, Chen YP, et al. Ethanol extract of *Rosa laevigata* michx. fruit inhibits inflammatory responses through NF- κ B/MAPK signaling pathways via AMPK activation in RAW 264.7 macrophages[J]. *Molecules*, 2023, 28(6): 2813.
- [24] Zhang TY, Sun WJ, Wang LX, et al. *Rosa laevigata* michx. polysaccharide ameliorates diabetic nephropathy in mice through inhibiting ferroptosis and PI3K/AKT pathway-mediated apoptosis and modulating tryptophan metabolism[J]. *J Diabetes Res*, 2023, 2023: 9164883.

Submission received: 2025-07-19/ Revised: 2025-08-08

· 论 著 ·

金胡固肾方治疗大量蛋白尿期糖尿病肾病患者 有效性及安全性的回顾性队列研究

付新智¹, 李奕璇¹, 刘传峰², 王颜刚¹

1. 青岛大学附属医院内分泌科, 山东 青岛 266003; 2. 青岛大学附属医院血液科, 山东 青岛 266003

摘要: **目的** 探讨金胡固肾方对大量蛋白尿期的糖尿病肾病(DKD)患者肾功能的影响,并评估其疗效和安全性。**方法** 对青岛大学附属医院内分泌科 2023 年 6 月至 2025 年 6 月收治的 88 例大量蛋白尿期 DKD 患者进行回顾性队列研究,依据治疗方案分为金胡固肾方组($n=43$)和非奈利酮组($n=45$)。比较两组患者的肾功能指标[尿蛋白/肌酐比值(UACR)、血肌酐、血尿酸、估算肾小球滤过率(eGFR)]和安全性指标(血钾)。**结果** 对于大量蛋白尿期 DKD 患者,金胡固肾方组治疗有效率略高于非奈利酮组,但差异无统计学意义[88.37%(38/43) vs 77.78%(35/45), $\chi^2=1.745$, $P=0.186$]。治疗后,金胡固肾方组血尿酸水平显著低于非奈利酮组[(340.51±87.06) $\mu\text{mol/L}$ vs (383.96±90.04) $\mu\text{mol/L}$, $t=2.301$, $P=0.024$],血尿酸下降率显著高于非奈利酮组(4.88%±24.98% vs -9.66%±25.09%, $t=2.724$, $P=0.008$)。安全性方面,金胡固肾方组治疗后血钾水平显著低于非奈利酮组[(4.59±0.34) mmol/L vs (4.94±0.47) mmol/L, $t=2.719$, $P=0.010$],血钾升高率显著低于非奈利酮组(-0.22%±8.34% vs 9.23%±8.60%, $t=3.529$, $P=0.001$)。**结论** 金胡固肾方具备和非奈利酮相近的降低大量蛋白尿期 DKD 患者 UACR 的效果,并能够更好地降低 DKD 患者血尿酸水平,且具有良好的安全性。

关键词: 糖尿病肾病; 金胡固肾方; 蛋白尿; 血尿酸; 血钾; 非奈利酮

中图分类号: R255.4 R587.2 **文献标识码:** A **文章编号:** 1674-8182(2025)09-1342-05

Effectiveness and safety of *Jinhu Gushen* Formula in diabetic kidney disease patients with massive proteinuria: a retrospective cohort study

FU Xinzhi*, LI Yixuan, LIU Chuanfeng, WANG Yangang

*Department of Endocrinology, The Affiliated Hospital of Qingdao University, Qingdao, Shandong 266003, China

Corresponding author: WANG Yangang, E-mail: wangyg1966@126.com

Abstract: Objective To investigate the effect of *Jinhu Gushen* Formula on renal function in diabetic kidney disease (DKD) patients with massive proteinuria, and to evaluate its efficacy and safety. **Methods** A retrospective cohort study was conducted on 88 DKD patients with massive proteinuria admitted to the Department of Endocrinology of the Affiliated Hospital of Qingdao University from June 2023 to June 2025. According to the treatment plan, the patients were divided into the *Jinhu Gushen* Formula group ($n=43$) and the finerenone group ($n=45$). Renal function indicators [urine albumin-to-creatinine ratio (UACR), serum creatinine, serum uric acid, estimated glomerular filtration rate (eGFR)] and safety indicators (serum potassium) between two groups of patients were compared. **Results** For DKD patients with massive proteinuria, the *Jinhu Gushen* Formula group demonstrated a lightly higher effective rate compared to the finerenone group, without significant statistical significance [88.37% (38/43) vs 77.78% (35/45), $\chi^2=1.745$, $P=0.186$]. The serum uric acid level in the *Jinhu Gushen* Formula group was significantly lower than that in the finerenone group [(340.51±87.06) $\mu\text{mol/L}$ vs (383.96±90.04) $\mu\text{mol/L}$, $t=2.301$, $P=0.024$], and the rate of uric acid reduction was significantly greater in the *Jinhu Gushen* Formula group (4.88%±24.98% vs -9.66%±25.09%, $t=2.724$, $P=0.008$). In terms of safety, the serum potassium level in the *Jinhu Gushen* Formula group was significantly lower than that in the

DOI:10.13429/j.cnki.cjcr.2025.09.009

基金项目: 国家科技重大专项(总项目编号:2024ZD0523500,子项目编号:2024ZD0523505)

通信作者: 王颜刚, E-mail: wangyg1966@126.com

出版日期: 2025-09-20



QR code for English version

finerenone group $[(4.59 \pm 0.34) \text{ mmol/L vs } (4.94 \pm 0.47) \text{ mmol/L}, t=2.719, P=0.010]$, with a significantly lower rate of potassium elevation observed in the *Jinhu Gushen* Formula group $(-0.22\% \pm 8.34\% \text{ vs } 9.23\% \pm 8.60\%, t=3.529, P=0.001)$. **Conclusion** *Jinhu Gushen* Formula has a similar effect as finerenone in reducing UACR in DKD patients with massive proteinuria, and can better reduce their blood uric acid levels, with good safety.

Keywords: Diabetic kidney disease; *Jinhu Gushen* Formula; Proteinuria; Serum uric acid; Serum potassium; Finerenone
Fund program: National Science and Technology Major Project (Overall Project Number: 2024ZD0523500, Sub-project Number: 2024ZD0523505)

近年来,随着全球糖尿病患病率逐渐上升,作为糖尿病重要微血管并发症的糖尿病肾病(diabetic kidney disease, DKD)显著加重了全球疾病负担^[1]。截至 2020 年,中国已有接近 1/3 的糖尿病患者患有 DKD^[2]。DKD 的发病严重影响糖尿病患者的长期预后与生活质量。目前临床对于 DKD 的治疗主要依赖血糖管理、血压控制和蛋白尿改善^[3-4]。非甾体盐皮质激素受体拮抗剂(non-steroidal mineralocorticoid receptor antagonist, ns-MRA)——非奈利酮,作为目前唯一降 DKD 患者蛋白尿的药物,在单药治疗和联合治疗中均扮演关键角色。近年来,中医药在 DKD 治疗中崭露头角,逐渐成为重要治疗手段。这一转变归因于中医药在治疗过程中的多靶点效应,同时这种多靶点效应与 DKD 进展相适应,发挥出中医药个体化、动态干预的特点,共同调节肾脏细胞遗传、氧化代谢和炎症反应的进展^[5]。金胡固肾方是青岛大学附属医院王颜刚教授为治疗 DKD 研制的中药复方,具有“扶阳固肾、益气养阴、健脾化痰”的功效。本研究旨在通过对比金胡固肾方与非奈利酮在降低 DKD 患者尿蛋白水平、改善肾功能等方面的疗效,以期推动中医药在 DKD 治疗中的应用,为 DKD 患者的临床治疗提供新的手段。

1 对象和方法

1.1 研究对象与分组 回顾性选取 2023 年 6 月至 2025 年 6 月于青岛大学附属医院内分泌科门诊就诊的 DKD 患者进行队列研究,总计 88 例,根据应用降蛋白尿药物分为金胡固肾方组(金胡固肾方+基础 DKD 治疗)和非奈利酮组(非奈利酮+基础 DKD 治疗)。本研究已获得青岛大学附属医院伦理委员会批准(伦理号:QYFY WZLL30229)。

1.2 纳入标准 (1) 年龄 ≥ 18 周岁, 身体质量指数(body mass index, BMI) $\leq 45 \text{ kg/m}^2$; (2) 符合《中国糖尿病肾脏病防治指南(2021 年版)》^[6]和《糖尿病肾脏病中西医结合防治专家共识(2023 版)》^[7]关于 DKD 大量蛋白尿期诊断; (3) 糖尿病病程 ≥ 5 年; (4) 历史

数据 ≥ 3 个月且病历资料完整者。

1.3 排除标准 (1) 近期发生过低血糖昏迷、糖尿病酮症酸中毒、乳酸中毒等糖尿病急性并发症; (2) 患有其他可能影响肾功能或尿蛋白排泄的疾病(如心力衰竭、心肌梗死、感染、免疫性疾病等),或其他恶性疾病(如恶性肿瘤等); (3) 初始尿白蛋白/肌酐比值(urine albumin-to-creatinine ratio, UACR) $< 30 \text{ mg/g}$; (4) 需要透析或肾移植治疗; (5) 治疗不规范,影响疗效评估。

1.4 治疗方案 (1) 金胡固肾方组: 采用金胡固肾方+基础 DKD 治疗, 金胡固肾方方剂组成为黄芪、麸炒白术、金樱子、刺五加、积雪草、石斛、丹参、葛根、川牛膝、女贞子、胡芦巴、桂枝、半枝莲、麸白芍、盐杜仲、三七粉。早晚各 1 次, 每次煎煮 250 mL, 餐后服用, 连续服用 3 个月。(2) 非奈利酮组: 采用非奈利酮+基础 DKD 治疗, 非奈利酮片(德国拜耳公司, 批号: 国药准字 HJ20220058, 20 mg/片), 每次 1 片, 每日 1 次, 连续服用 3 个月。治疗期间各组降糖、降压、降血脂治疗方案不变(用药剂量及频次遵照说明书, 无超说明书用药; 胰岛素维持剂量波动不超 10%)。

1.5 观察指标

1.5.1 一般资料 收集一般资料包括: 患者年龄、性别、糖尿病病程、BMI、治疗前 UACR、估算肾小球滤过率(estimated glomerular filtration rate, eGFR)、血钾、血肌酐、血尿酸、空腹血糖(fasting blood glucose, FBG)、血脂[三酰甘油(triglycerides, TG)、低密度脂蛋白(low density lipoprotein, LDL)]、糖化血红蛋白(glycated hemoglobin, HbA_{1c})、药物治疗方案等。

1.5.2 疗效与安全性指标 主要疗效指标包括 UACR、血肌酐、血尿酸。次要疗效指标包括 eGFR。安全性指标为血钾水平。

1.5.3 临床疗效指标 (1) UACR 下降率; (2) 治疗有效率(UACR 降至正常范围或降低超过基线水平 30% 则认为治疗有效); (3) 治疗有效程度: 有效、显著有效及无效患者的构成比(相对基线水平降低 $\geq$

30%且<50%认为治疗有效,比基线水平降低≥50%认为治疗显著有效,其他情况视为无效)^[8]。

1.6 统计学方法 采用 R4.5.0 软件进行统计学处理。正态分布的计量资料检验方差齐性后各以 $\bar{x}\pm s$ 表示,组间比较使用 t 检验。非正态分布的计量资料以 $M(P_{25},P_{75})$ 表示,比较使用 Wilcoxon 秩和检验。计数资料以例(%)表示,组间比较使用 χ^2 检验,有序等级资料比较采用秩和检验。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者的一般资料分析 本研究共纳入患者 88 例。金胡固肾方组 43 例,非奈利酮组 45 例。两组患者的年龄、性别、糖尿病病程、BMI、FBG、HbA_{1c}、TG、LDL 和药物治疗方案等指标差异均无统计学意义($P>0.05$)。见表 1。

2.2 两组疗效比较 在大量蛋白尿(UACR≥300 mg/g)患者中,金胡固肾方组治疗有效率与非奈利酮组相近[88.37%(38/43) vs 77.78%(35/45), $\chi^2=1.745$, $P=0.186$],两组治疗有效程度比较见表 2。金胡固肾方组治疗后血尿酸水平显著低于非奈利酮组($P<0.05$),两组 UACR、血肌酐、eGFR 水平比较差异无统计学意义($P>0.05$)。金胡固肾方组血尿酸下降率显著高于非奈利酮组($4.88\%\pm 24.98\%$ vs $-9.66\%\pm 25.09\%$, $t=2.724$, $P=0.008$),但 UACR 下降率($51.68\%\pm 16.20\%$ vs $46.18\%\pm 18.28\%$, $t=1.496$, $P=0.138$)、血肌酐下降率($2.81\%\pm 14.18\%$ vs $1.28\%\pm 15.19\%$, $t=0.491$, $P=0.625$)、eGFR 升高率($1.93\%\pm 9.18\%$ vs $-3.95\%\pm 10.75\%$, $t=1.859$, $P=0.071$)差异无统计学意义。两组治疗前后肾功能比较,见表 3。

2.3 两组安全性比较 治疗前金胡固肾方组血钾水平与非奈利酮组差异无统计学意义[(4.62±0.43) mmol/L vs (4.54±0.43) mmol/L, $t=0.599$, $P=0.553$],治疗后金胡固肾方组血钾水平显著低于非奈利酮组[(4.59±0.34) mmol/L vs (4.94±0.47) mmol/L, $t=2.719$, $P=0.010$],血钾升高率金胡固肾方组显著低于非奈利酮

组($-0.22\%\pm 8.34\%$ vs $9.23\%\pm 8.60\%$, $t=3.529$, $P=0.001$)。

表 1 两组患者一般资料比较
Tab.1 Comparison of general data between two groups of patients

指标	金胡固肾方组 (n=43)	非奈利酮组 (n=45)	χ^2 值	P 值
年龄(岁) ^a	60.93±13.19	62.18±12.37	0.457	0.649
男性[例(%)]	30(69.77)	29(64.44)	0.093	0.761
糖尿病病程(年) ^a	16.30±10.46	15.82±8.15	0.239	0.812
BMI(kg/m ²) ^a	25.48±3.83	25.47±3.19	0.012	0.991
生化指标				
FBG(mmol/L) ^a	7.29±1.92	6.93±1.92	0.890	0.376
HbA _{1c} (%) ^a	7.77±1.57	7.49±1.34	0.922	0.359
TG(mmol/L) ^a	1.43±0.72	1.46±0.65	0.179	0.858
LDL(mmol/L) ^a	2.71±0.82	2.52±1.02	0.938	0.351
降糖药物[例(%)]				
GLP-1RA	6(13.95)	11(24.44)	0.953	0.329
胰岛素	23(53.49)	22(48.89)	0.048	0.827
二甲双胍	14(32.56)	17(37.78)	0.084	0.772
α-糖苷酶抑制剂	7(16.28)	12(26.67)	0.855	0.355
DPP-4 抑制剂	20(46.51)	24(53.33)	0.182	0.670
噻唑烷二酮类	7(16.28)	4(8.89)	0.526	0.468
SGLT-2i	27(62.79)	30(66.67)	0.025	0.875
磺脲类	8(18.60)	5(11.11)	0.476	0.490
降压药[例(%)]				
ACEI/ARB	25(58.14)	21(48.89)	0.430	0.512
CCB	18(41.86)	22(48.89)	0.200	0.654
利尿剂	8(18.60)	4(8.89)	1.034	0.309
降脂药[例(%)]				
他汀类	19(44.19)	22(48.89)	0.052	0.819
贝特类	4(9.30)	1(2.22)	0.948	0.330
其他保肾药物	19(44.19)	22(48.89)	0.052	0.819

注:^a为数据以 $\bar{x}\pm s$ 表示。GLP-1RA 为胰高糖素样肽-1 受体激动剂;DPP-4 为二肽基肽酶-4;SGLT-2i 为钠-葡萄糖协同转运蛋白 2 抑制剂;ACEI 为血管紧张素转化酶抑制剂;ARB 为血管紧张素受体拮抗剂;CCB 为钙通道阻滞剂。

表 2 两组疗效比较 [例(%)]
Tab.2 Comparison of therapeutic effect between two groups [case(%)]

组别	显著有效	有效	无效
金胡固肾方组(n=43)	22(51.16)	16(37.21)	5(11.63)
非奈利酮组(n=45)	18(40.00)	17(37.78)	10(22.22)
Z 值		1.319	
P 值		0.202	

表 3 金胡固肾方组与非奈利酮组治疗前后肾功能指标比较
Tab.3 Comparison of renal function indicators before and after treatment between the Jinhu Gushen Formula group and the finerenone group

组别	UACR[M(P ₂₅ ,P ₇₅)]		血尿酸(μmol/L, $\bar{x}\pm s$)		血肌酐(μmol/L, $\bar{x}\pm s$)		eGFR[mL/(min·1.73 m ²), $\bar{x}\pm s$]	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
金胡固肾方组 (n=43)	916.24 (490.15,1 453.64)	337.88 (237.78,693.33)	376.77±113.49	340.51±87.06	82.34±25.66	80.00±27.78	86.48±16.94	88.31±19.25
非奈利酮组 (n=45)	938.58 (530.03,1 557.40)	538.58 (269.67,803.92)	363.98±98.61	383.96±90.04	84.11±25.79	82.73±28.74	81.27±16.17	78.41±18.56
Z/t 值	7.379	6.832	0.563	2.301	0.323	0.454	0.994	1.656
P 值	0.787	0.728	0.575	0.024	0.748	0.651	0.326	0.106

3 讨论

尽管近年来多种药物均被证实能够延缓 DKD 患者肾脏病进展^[9],但仍有部分患者肾功能持续恶化,亟需新药提供更有效的治疗。近年中医药在 DKD 的治疗中逐渐展现出巨大潜力^[5]。糖尿病患者经过多年高血糖、血脂紊乱、高血压的影响,肾脏组织发生虚损变化。金胡固肾方系在中医理论指导下,以扶阳固肾为核心功效,经多年临床实践总结凝练的固定成方。本团队前期研究对比了金胡固肾方与黄葵胶囊的临床疗效,证实了金胡固肾方对 DKD 患者肾脏功能的改善作用^[10]。本研究进一步采用回顾性队列研究方法,将金胡固肾方与非奈利酮做对比,旨在评估其在 DKD 治疗中的有效性与安全性。

非奈利酮作为新一代 ns-MRA,经过两项 III 期临床试验^[11-12]的探索,目前在多国指南中均被推荐为延缓 DKD 进展的优秀治疗药物^[6-7,13]。UACR 近年来已成为衡量药物对慢性肾病治疗效果的关键指标^[14-16]。本研究结果显示,金胡固肾方组治疗有效率高于非奈利酮组(88.37% vs 77.78%),但差异无统计学意义,这可能与本研究样本量不足有关。尽管如此,本研究仍表明,大量蛋白尿期 DKD 患者使用金胡固肾方治疗能达到与非奈利酮相近的降低 UACR 的效果。此外有研究指出,降低血尿酸有助于延缓 DKD 进展并改善患者长期预后^[17],因此本研究将血尿酸列为主要结局指标之一。组间比较显示两组血尿酸指标变化差异有统计学意义,大量蛋白尿期 DKD 患者使用金胡固肾方治疗后血尿酸水平总体呈稳定下降趋势;同时金胡固肾方组血尿酸下降率显著高于非奈利酮组,表明其血尿酸控制效果更优。非奈利酮的高钾血症相关不良事件发生率较高^[12,18],限制了其临床应用。本研究发现,在使用金胡固肾方的 DKD 患者中,血钾水平在 3 个月的随访期间保持安全范围,血钾升高率低于使用非奈利酮治疗的患者。综合以上结果,金胡固肾方在改善肾功能方面与非奈利酮相近,同时在稳定患者血钾、改善 DKD 患者高尿酸状态方面具有独特优势,潜在适用人群更广,上述发现将为大量蛋白尿期 DKD 患者提供新的临床治疗手段。

近年来的研究显示,DKD 患者出现蛋白尿增多和肾功能下降与肾脏足细胞凋亡和功能受损、肾小球基底膜炎症性增厚密切相关^[19-20]。目前的基础研究显示,金胡固肾方主要成分金樱子和葫芦巴表现出了较强的抗氧化、抗炎活性^[21-22]。二者联合通过抑

制丝裂原活化蛋白激酶(p38 mitogen-activated protein kinase, MAPK)/核因子 κ B(nuclear factor kappa-B, NF- κ B)信号通路^[23]、调节色氨酸代谢^[24]、调节磷脂酰肌醇 3 激酶(phosphatidylinositol-3-kinase, PI3K)/蛋白激酶 B(protein kinase B)/细胞外信号调节激酶(extracellular regulated protein kinases, ERK)信号通路和脂质代谢通路^[21]等多种途径实现肾脏保护作用。

本研究存在局限性。首先,本研究随访时间较短,金胡固肾方的早期疗效是否能改善长期预后值得更深入的探索研究。同时本研究为单中心回顾性研究,患者普适性有限,未来需要进行多中心大样本前瞻性研究来进一步验证本研究结论,以推进金胡固肾方在 DKD 治疗中的临床应用。

综合上述研究结果,在 DKD 患者治疗过程中,金胡固肾方展现出和非奈利酮近似的降 UACR 效果,同时能降低血尿酸水平,血钾升高不良反应发生率低,安全性好。

利益冲突 所有作者声明不存在利益冲突

参考文献

- [1] Fenta ET, Eshetu HB, Kebede N, et al. Prevalence and predictors of chronic kidney disease among type 2 diabetic patients worldwide, systematic review and meta-analysis [J]. *Diabetol Metab Syndr*, 2023, 15(1): 245.
- [2] Jia WP, Yu R, Wang LM, et al. Prevalence of chronic kidney disease among Chinese adults with diabetes: a nationwide population-based cross-sectional study [J]. *Lancet Reg Health West Pac*, 2025, 55: 101463.
- [3] Naaman SC, Bakris GL. Diabetic nephropathy: update on pillars of therapy slowing progression [J]. *Diabetes Care*, 2023, 46(9): 1574-1586.
- [4] Zhao MM, Cao YT, Ma L. New insights in the treatment of DKD: recent advances and future prospects [J]. *BMC Nephrol*, 2025, 26(1): 72.
- [5] Cai RS, Li CY, Zhao Y, et al. Traditional Chinese medicine in diabetic kidney disease: multifaceted therapeutic mechanisms and research progress [J]. *Chin Med*, 2025, 20(1): 95.
- [6] 中华医学会糖尿病学分会微血管并发症学组. 中国糖尿病肾脏病防治指南(2021 年版) [J]. *中华糖尿病杂志*, 2021, 13(8): 762-784.
- [7] 中国中西医结合学会内分泌专业委员会糖尿病肾脏病专家委员会, 中国微循环学会中医与微循环专业委员会. 糖尿病肾脏病中西医结合防治专家共识(2023 版) [J]. *中华糖尿病杂志*, 2023, 15(8): 690-702.
- [8] Mentz RJ, Anker SD, Pitt B, et al. Efficacy and safety of finerenone in patients with chronic kidney disease and type 2 diabetes by diuretic use: a FIDELITY analysis [J]. *Eur J Heart Fail*, 2025, 27(5): 764-774.
- [9] Yamazaki T, Mimura I, Tanaka T, et al. Treatment of diabetic kidney disease: current and future [J]. *Diabetes Metab J*, 2021, 45(1): 11-26.
- [10] 李奕璇, 黄雅静, 魏凡翔, 等. 金胡固肾方降低糖尿病肾病患者尿蛋白及血尿酸的临床疗效分析 [J]. *精准医学杂志*, 2025, 40(2): 102-107.

(下转第 1349 页)

现,与对照组比较,联合组炎症因子水平更低,提示肾衰宁片联合达格列净治疗可以抑制炎症反应。大黄提取物能够抑制炎症因子表达;太子参可以增强机体免疫力,发挥抗炎效果;丹参具有一定的抗炎作用。治疗期间,两组副作用发生率比较无明显差异,提示肾衰宁片治疗不会增加药物副作用,安全性好。

综上所述,对于Ⅲ~Ⅳ期2型糖尿病合并DKD患者,采用肾衰宁片联合达格列净治疗能增强疗效、改善肾功能、降低血脂和减轻炎症反应,且安全性好,是一种较好的治疗方案。

利益冲突 无

参考文献

- [1] Ueki K, Sasako T, Okazaki Y, et al. Multifactorial intervention has a significant effect on diabetic kidney disease in patients with type 2 diabetes[J]. *Kidney Int*, 2021, 99(1): 256-266.
- [2] 李惠, 刘建林, 牛聪, 等. 益肾化湿颗粒治疗糖尿病肾病的效果及对肾小管损伤的影响[J]. *罕少疾病杂志*, 2020, 27(3): 51-54.
- [3] 虞天璇, 王琛. 消白衍生方治疗糖尿病肾病Ⅲ-Ⅳ期患者尿蛋白的疗效观察[J]. *世界中西医结合杂志*, 2023, 18(7): 1396-1400.
- [4] 刘珊珊, 张帆, 孙丽丽, 等. 益气养血活血法联合达格列净对糖尿病肾病肾小球滤过功能、血糖及NO/ET平衡的影响[J]. *四川中医*, 2023, 41(10): 131-136.
- [5] 王泉蓉, 于洪洁. 益气通络消癥方对糖尿病肾病患者肾功能及尿足细胞损伤标志物的影响[J]. *临床与病理杂志*, 2023, 43(3): 469-476.
- [6] 陈杰彬, 胡蓉, 李成杰, 等. 肾衰宁片联合左卡尼汀对慢性肾脏病3-4期患者的疗效[J]. *实用医学杂志*, 2022, 38(13): 1671-1675.
- [7] 中华医学会糖尿病学分会. 中国2型糖尿病防治指南(2017年版)[J]. *中国实用内科杂志*, 2018, 38(4): 292-344.
- [8] 中华医学会内分泌学分会. 中国成人糖尿病肾脏病临床诊断的专家共识[J]. *中华内分泌代谢杂志*, 2015, 31(5): 379-385.
- [9] 杨霓芝, 刘旭生. 糖尿病肾病诊断、辨证分型及疗效评定标准(试行方案)[J]. *上海中医药杂志*, 2007, 41(7): 7-8.
- [10] Barrera-Chimal J, Lima-Posada I, Bakris GL, et al. Mineralocorticoid receptor antagonists in diabetic kidney disease - mechanistic and therapeutic effects[J]. *Nat Rev Nephrol*, 2022, 18(1): 56-70.
- [11] Wang H, Liu DW, Zheng B, et al. Emerging role of ferroptosis in diabetic kidney disease: molecular mechanisms and therapeutic opportunities[J]. *Int J Biol Sci*, 2023, 19(9): 2678-2694.
- [12] 郭永榜, 张晓亚, 郭青榜, 等. BOLD MRI对2型糖尿病肾病患者肾功能损伤的评估价值研究[J]. *中国CT和MRI杂志*, 2022, 20(4): 121-123, 168.
- [13] 黄程, 邵云侠, 吴艳, 等. 骨化三醇联合奥美沙坦酯治疗早期2型糖尿病肾病的效果及对肾病足细胞损伤的机制探讨[J]. *中国医药导报*, 2022, 19(15): 79-82.
- [14] 江铭倩, 叶彬华, 任莎莉, 等. 益肾降糖饮治疗糖尿病肾病Ⅲ期气阴两虚证的临床疗效及对ROS-NLRP3-IL-1 β 信号通路的影响[J]. *中医导报*, 2022, 28(2): 61-65.
- [15] 李仁武, 刘宝利, 纪利梅, 等. 肾衰宁颗粒联合甘精胰岛素对糖尿病肾病患者肾功能、血糖及氧化应激的影响[J]. *现代生物医学进展*, 2021, 21(14): 2726-2729.
- [16] 沈金峰, 胡良伟, 胡芳, 等. 健脾益肾养阴方治疗2型糖尿病肾病Ⅳ期患者的临床疗效分析[J]. *中医药信息*, 2021, 38(5): 65-68.
- [17] 蒋婷婷, 曾渊杰, 费梅. 黄葵胶囊联合西药治疗糖尿病肾病Ⅲ、Ⅳ期疗效及其抑制肾组织氧化应激机制探究[J]. *世界中西医结合杂志*, 2021, 16(12): 2320-2324, 2328.
- [18] 罗璇, 韦少恒, 韦珍红. 肾衰宁胶囊联合阿托伐他汀治疗糖尿病肾病的临床效果[J]. *广西医学*, 2022, 44(13): 1462-1466.
- [19] 单鸿, 吴雁翔. 肾衰宁胶囊联合替米沙坦对糖尿病肾病患者血管内皮功能及炎症因子水平的影响[J]. *成都医学院学报*, 2022, 17(1): 67-70.
- 收稿日期:2025-03-12 修回日期:2025-04-27 编辑:王国品
- [11] Pitt B, Filippatos G, Agarwal R, et al. Cardiovascular events with finerenone in kidney disease and type 2 diabetes [J]. *N Engl J Med*, 2021, 385(24): 2252-2263.
- [12] Bakris GL, Agarwal R, Anker SD, et al. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes [J]. *N Engl J Med*, 2020, 383(23): 2219-2229.
- [13] American Diabetes Association Professional Practice Committee. Chronic kidney disease and risk management: standards of care in diabetes-2025[J]. *Diabetes Care*, 2025, 48(1 Suppl 1): S239-S251.
- [14] Liu D, Lv LL. New understanding on the role of proteinuria in progression of chronic kidney disease [J]. *Adv Exp Med Biol*, 2019, 1165: 487-500.
- [15] 杨飞, 邵小娟, 霍媛媛, 等. 糖尿病足患者血清胆红素水平与UACR的相关性[J]. *热带医学杂志*, 2024, 24(9): 1283-1288.
- [16] 陈久应, 徐新润, 宰国田, 等. 2型糖尿病患者血浆低密度脂蛋白亚型水平与糖尿病肾病的相关性[J]. *中国临床研究*, 2023, 36(3): 445-449.
- [17] Mauer M, Doria A. Uric acid and risk of diabetic kidney disease [J]. *J Nephrol*, 2020, 33(5): 995-999.
- [18] Agarwal R, Filippatos G, Pitt B, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis [J]. *Eur Heart J*, 2022, 43(6): 474-484.
- [19] Mohandes S, Doke T, Hu H, et al. Molecular pathways that drive diabetic kidney disease [J]. *J Clin Invest*, 2023, 133(4): e165654.
- [20] Antar SA, Ashour NA, Sharaky M, et al. Diabetes mellitus: classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments [J]. *Biomed Pharmacother*, 2023, 168: 115734.
- [21] Niu Y, Niu HJ, Chi LX, et al. *Trigonella foenum-graecum* L. protects against renal function decline in a mouse model of type 2 diabetic nephropathy by modulating the PI3K-Akt-ERK signaling pathway [J]. *Front Pharmacol*, 2025, 16: 1566723.
- [22] Chen S, Wang L, Rong S, et al. Extraction, purification, chemical characterization, and *in vitro* hypoglycemic activity of polysaccharides derived from *Rosa laevigata Michx* [J]. *Int J Biol Macromol*, 2024, 279(Pt 1): 135116.
- [23] Wu HT, Lin TT, Chen YP, et al. Ethanol extract of *Rosa laevigata Michx*. fruit inhibits inflammatory responses through NF- κ B/MAPK signaling pathways *via* AMPK activation in RAW 264.7 macrophages [J]. *Molecules*, 2023, 28(6): 2813.
- [24] Zhang TY, Sun WJ, Wang LX, et al. *Rosa laevigata Michx*. polysaccharide ameliorates diabetic nephropathy in mice through inhibiting ferroptosis and PI3K/AKT pathway-mediated apoptosis and modulating tryptophan metabolism [J]. *J Diabetes Res*, 2023, 2023: 9164883.
- 收稿日期:2025-07-19 修回日期:2025-08-08 编辑:叶小舟

(上接第1345页)