

Risk factors for diabetic kidney disease and the interaction between glycemic variability and systolic blood pressure in young overweight/obese patients with type 2 diabetes: a retrospective cross-sectional study

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Abstract

Background

Young overweight or obese patients with type 2 diabetes mellitus develop diabetic kidney disease earlier than middle-aged and elderly patients. However, large-sample studies in this population are lacking, and whether systolic blood pressure modifies the association between glycemic variability and diabetic kidney disease remains unclear.

Methods

A total of 3162 overweight or obese inpatients with type 2 diabetes mellitus aged 18–45 years were retrospectively enrolled between January 2017 and December 2022 and divided into a non-diabetic kidney disease group ($n = 1661$) and a diabetic kidney disease group ($n = 1501$) according to the urinary albumin-to-creatinine ratio. Multivariate logistic regression was used to identify independent risk factors for diabetic kidney disease. Multiplicative interaction was assessed using a centered product term, and additive interaction was evaluated using the relative excess risk due to interaction, attributable proportion due to interaction, and synergy index. Subgroup analyses were stratified by systolic blood pressure and body mass index.

Results

Multivariate logistic regression showed that glycemic variability ($OR = 10.717$, 95% CI 4.089–28.089), obesity ($OR = 6.630$, 95% CI 5.608–7.838), systolic blood pressure ($OR = 1.020$, 95% CI 1.012–1.027), low educational level ($OR = 2.025$, 95% CI 1.713–2.393), antihypertensive drug use ($OR = 2.256$, 95% CI 1.860–2.737), total cholesterol ($OR = 1.135$, 95% CI 1.061–1.214), and serum uric acid ($OR = 1.002$, 95% CI 1.001–1.003) were independent risk factors for diabetic kidney disease ($P < 0.05$). A multiplicative interaction was observed between glycemic variability and systolic blood pressure (interaction $OR = 1.073$, 95% CI 1.005–1.147, $P = 0.036$); additive interaction did not reach statistical significance. Stratified analysis showed that glycemic variability was not significantly associated with diabetic kidney disease when systolic blood pressure was normal, whereas a significant association was observed when systolic blood pressure was ≥ 130 mmHg ($P < 0.01$).

Conclusions

Elevated glycemic variability is a core independent risk factor for diabetic kidney disease in young overweight or obese patients with type 2 diabetes mellitus and exhibits a multiplicative interaction with systolic blood pressure. Elevated systolic blood pressure may amplify glycemic variability-related kidney

injury. Clinical management should combine stable glucose control with blood pressure reduction according to systolic blood pressure stratification.

Introduction

In recent years, the prevalence of type 2 diabetes mellitus (T2DM) has continued to rise, making it a major global public health problem^[1]. Compared with middle-aged and elderly patients, young overweight or obese individuals with T2DM develop microvascular complications earlier and experience faster disease progression. Diabetic kidney disease (DKD), the most common microvascular complication, is the leading cause of end-stage renal disease and substantially increases the risk of disability and mortality^[2]. Obesity can mediate glomerular injury through multiple pathways, including insulin resistance, overactivation of the renin–angiotensin–aldosterone system, chronic low-grade inflammation, and oxidative stress, and is a well-recognized risk factor for DKD^[3].

Beyond obesity, glycemic variability is also considered an important risk factor for DKD. The coefficient of variation (CV) of glucose accurately reflects the amplitude of short-term glycemic fluctuations, and its renal injurious effects are independent of static indicators such as glycated hemoglobin and mean blood glucose. Marked glycemic fluctuations can activate oxidative stress, damage glomerular vascular endothelium, promote the release of pro-inflammatory cytokines, and accelerate glomerulosclerosis^[4]. Elevated systolic blood pressure (SBP), in turn, increases glomerular capillary hydrostatic pressure, causing glomerular hyperfiltration and mechanical injury^[5]. Glycemic variability can impair vascular endothelium and reduce vascular compliance, while elevated SBP can further increase the glomerular filtration load; theoretically, the two may exert a synergistic effect on renal injury. Existing studies on glycemic variability and DKD have mostly focused on middle-aged and elderly patients with T2DM, and large-sample studies in young overweight or obese populations are lacking. Moreover, most studies have used static glycemic indicators such as glycated hemoglobin and fasting glucose, and whether SBP modifies the association between glycemic variability and renal injury remains unclear.

This study retrospectively analyzed the clinical data of young overweight or obese inpatients with T2DM, identified independent risk factors for DKD, quantified the interaction between CV and SBP, and examined whether SBP modifies the association between CV and DKD, to provide evidence for individualized clinical management.

1 Subjects and Methods

1.1 General Information

This was a retrospective cross-sectional analysis based on inpatient medical records, with DKD as the outcome variable for group comparison. Clinical data were collected from patients aged 18–45 years with overweight or obesity and T2DM who were hospitalized in multiple endocrinology-related wards of the First Affiliated Hospital of Henan University of Science and Technology between January 2017 and

December 2022. A total of 3,162 patients meeting the inclusion criteria were finally enrolled, including 1,501 in the DKD group and 1,661 in the non-DKD group. This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Henan University of Science and Technology (approval number: 2025 – 0275), and all participants provided informed consent.

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) meeting the diagnostic criteria for diabetes in the Chinese Guidelines for the Prevention and Treatment of Diabetes (2024 Edition)^[6]; (2) age 18–45 years; (3) body mass index (BMI) $\geq 24.0 \text{ kg/m}^2$ ^[7]; (4) complete data on continuous glucose monitoring, UACR, blood pressure, blood lipids, and demographics.

Exclusion criteria: (1) acute stress states such as diabetic ketoacidosis, hyperosmolar hyperglycemic state, or a history of infection or surgery within the past 4 weeks; (2) renal damage caused by other conditions, such as primary glomerular disease or lupus nephritis; (3) pregnant or lactating women.

Diagnosis and grouping of DKD: According to the *National Technical Guidelines for the Prevention and Treatment of Diabetic Kidney Disease at the Primary Care Level (2023)*^[8], patients with UACR $\geq 30 \text{ mg/g}$ were assigned to the DKD group, and those with UACR $< 30 \text{ mg/g}$ to the non-DKD group.

Based on the above inclusion and exclusion criteria, a total of 4,453 inpatients aged 18–45 years with overweight/obesity and T2DM were initially screened. Of these, 541 were excluded for incomplete clinical data, 350 for acute stress states within the past 4 weeks, 111 for renal damage caused by other conditions, and 289 for pregnancy or lactation. Finally, 3,162 patients were included in the analysis, comprising 1,501 in the DKD group and 1,661 in the non-DKD group. The patient selection process is shown in Fig. 1.

1.3 Variable Definitions and Assignment

Clinical data of the study participants were collected through the hospital electronic medical record system. Outcome variable: DKD (UACR $\geq 30 \text{ mg/g}$). Core exposure variables: CV (continuous variable) and SBP (continuous variable). Confounding covariates: demographic characteristics (age, sex, educational level), anthropometric measures (BMI and BMI category), glycemic metabolic indicators (glycated hemoglobin, biochemical glucose, mean blood glucose, pre-breakfast blood glucose, number of episodes with blood glucose $> 20 \text{ mmol/L}$, number of episodes with blood glucose $< 3.9 \text{ mmol/L}$), insulin resistance indicators (fasting insulin, HOMA-IR, fasting C-peptide), blood pressure indicators (diastolic blood pressure), renal function indicators (serum creatinine), lipid metabolic indicators (total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol), serum uric acid, and treatment regimens (antihypertensive drugs, lipid-lowering drugs).

Assignment of categorical variables: sex (male = 1, female = 0); educational level (middle school or below = 1, high school/college/undergraduate = 0). The rationale for assigning low educational level as 1

was that these patients have poorer self-management ability and treatment adherence, and the cumulative renal injury risk from long-term metabolic disturbances is higher^[9]; BMI category (overweight = 0, obesity = 1); antihypertensive drug use (yes = 1, no = 0); lipid-lowering drug use (yes = 1, no = 0).

Variable grouping cutoffs: SBP stratification (normal < 130 mmHg, borderline 130–139 mmHg, hypertension $\geq$ 140 mmHg) according to the *Chinese Guidelines for the Prevention and Treatment of Hypertension (2024 Revision)^[10]; CV was dichotomized into high and low groups using the median of 0.37 in this cohort as the cutoff.

1.4 Statistical Analysis

Data analysis was performed using SPSS 29.0. Normally distributed continuous variables are presented as mean $\pm$ standard deviation and compared using the independent-samples t-test; non-normally distributed continuous variables are presented as median (interquartile range) and compared using the Mann–Whitney U test; categorical variables are presented as counts (%) and compared using the χ^2 test. Univariate and multivariate logistic regression analyses were used to identify factors associated with DKD. Variables with $P < 0.05$ in univariate analysis were entered into the multivariate model using the Enter method, with collinearity diagnostics performed before entry ($VIF < 10$). To reduce multicollinearity between the interaction term and the main effects, CV and SBP were mean-centered before constructing the product term, which was included in the logistic regression model to assess multiplicative interaction. RERI, API, and S were used to assess additive interaction. Subgroup analyses were performed by BMI and SBP strata; the BMI-stratified model was adjusted for SBP, whereas the SBP-stratified model was not, with all other adjustment variables the same as in the main model. $P < 0.05$ was considered statistically significant.

2 Results

2.1 Comparison of baseline characteristics between the two groups

BMI, SBP, CV, serum uric acid, and total cholesterol were higher in the DKD group than in the non-DKD group, and the proportions of patients with low educational level and antihypertensive drug use were also higher in the DKD group ($P < 0.05$). There were no statistically significant differences in sex, diastolic blood pressure, triglycerides, or low-density lipoprotein cholesterol between the two groups ($P > 0.05$) (Table 1). The line graph showed that mean blood glucose at each time point was higher in the DKD group than in the non-DKD group (Fig. 2).

Table 1
Comparison of baseline clinical characteristics among young overweight/obese inpatients with type 2 diabetes mellitus stratified by DKD status

Variable	Non-DKD group (n = 1661)	DKD group (n = 1501)	Test statistic	P
Demographic characteristics				
Age (years)	34.71 ± 4.01	35.01 ± 3.58	t = 2.212	0.027
Sex [n (%)]			$\chi^2 = 0.630$	0.428
Male	955 (57.50)	842 (56.10)		
Female	706 (42.50)	659 (43.90)		
Low educational level [n (%)]	749 (45.10)	937 (62.90)	$\chi^2 = 98.431$	< 0.01
Anthropometric indices				
BMI (kg/m ²)	27.75 ± 2.41	29.05 ± 2.75	t = 14.074	< 0.01
BMI classification [n (%)]			$\chi^2 = 600.137$	< 0.01
Overweight	1215 (73.10)	444 (29.60)		
Obesity	446 (26.90)	1057 (70.40)		
Glycemic metabolic indicators				
Glycated hemoglobin (%)	9.50 (7.80, 11.30)	9.35 (7.80, 10.80)	Z = -1.640	0.101
Biochemical glucose (mmol/L)	7.47 (5.60, 9.96)	8.09 (5.95, 11.22)	Z = 2.311	0.021
MBG (mmol/L)	9.10 (8.16, 10.02)	9.58 (8.50, 10.54)	Z = 4.757	< 0.01
CV (%)	0.35 (0.30, 0.41)	0.37 (0.31, 0.46)	Z = 3.831	< 0.01
Count of blood glucose > 20 mmol/L	2.00 (1.00, 4.00)	6.00 (2.00, 12.00)	Z = 4.685	< 0.01
Count of blood glucose < 3.9 mmol/L	1.00 (1.00, 3.00)	2.00 (1.00, 3.00)	Z = 2.571	0.010
Blood pressure indicators				
SBP (mmHg)	126.57 ± 12.88	132.63 ± 13.15	t = 13.086	< 0.01
Diastolic blood pressure (mmHg)	79.23 ± 7.32	79.25 ± 7.81	t = 0.087	0.931

Variable	Non-DKD group (n = 1661)	DKD group (n = 1501)	Test statistic	P
Pulse rate (times/min)	78.00 (75.00, 81.00)	78.00 (75.00, 81.00)	Z = 2.709	0.007
Treatment regimens				
Antihypertensive medication use [n (%)]	690 (41.50)	999 (66.60)	$\chi^2 = 198.271$	< 0.01
Lipid-lowering medication use [n (%)]	1059 (63.80)	1081 (72.00)	$\chi^2 = 24.604$	< 0.01
Renal function indicators				
Serum creatinine ($\mu\text{mol/L}$)	77.80 (41.00, 127.10)	123.00 (63.00, 223.00)	Z = -34.232	< 0.01
Estimated glomerular filtration rate (mL/min/1.73 m ²)	114.00 (104.00, 124.00)	111.00 (100.00, 124.00)	Z = -2.470	0.014
Serum uric acid ($\mu\text{mol/L}$)	294.00 (236.00, 358.00)	303.00 (244.00, 365.00)	Z = 7.417	< 0.01
Lipid metabolic indicators				
Total cholesterol (mmol/L)	4.34 (3.57, 5.07)	4.03 (3.31, 5.13)	Z = 2.845	0.004
Triglycerides (mmol/L)	1.51 (1.10, 2.23)	1.49 (1.10, 2.10)	Z = 1.055	0.291
High-density lipoprotein cholesterol (mmol/L)	1.00 (0.85, 1.19)	1.09 (0.95, 1.26)	Z = 2.906	0.004
Low-density lipoprotein cholesterol (mmol/L)	2.36 (1.83, 2.92)	1.82 (1.40, 2.58)	Z = -0.352	0.725

Note for Table 1: t value for independent-samples t-test; χ^2 value for chi-square test; Z value for Mann–Whitney U test.

2.2 Multivariate Logistic Regression Analysis of Influencing Factors for DKD

Collinearity diagnostics showed that the variance inflation factor (VIF) of all independent variables included in the multivariate model ranged from 1.050 to 1.936, all less than 10. Pearson correlation analysis revealed that the correlation coefficients between variables ranged from 0.115 to 0.532, all below 0.7, indicating no severe multicollinearity. Multivariate logistic regression demonstrated that coefficient of glycemic variability, obesity, systolic blood pressure, low educational level, antihypertensive medication use, total cholesterol, and serum uric acid were independent risk factors for DKD (all $P < 0.05$). These results are presented in Table 2. Univariate analysis results are shown in Supplementary Table S1.

Table 2
Multivariate Logistic Regression Analysis of Independent Risk Factors for DKD among Young Overweight/Obese Inpatients with Type 2 Diabetes Mellitus

Variable	B	SE	Wald χ^2	P	OR (95% CI)
Educational level (Higher education as reference)	0.705	0.085	68.369	< 0.01	2.025 (1.713–2.393)
BMI classification (Overweight as reference)	1.892	0.085	490.962	< 0.01	6.630 (5.608–7.838)
SBP	0.020	0.004	27.275	< 0.01	1.020 (1.012–1.027)
CV	2.372	0.492	23.278	< 0.01	10.717 (4.089–28.089)
Total cholesterol	0.127	0.034	13.663	< 0.01	1.135 (1.061–1.214)
Serum uric acid	0.002	0.001	23.222	< 0.01	1.002 (1.001–1.003)
Antihypertensive medication use (No use as reference)	0.814	0.099	68.148	< 0.01	

Note for Table 2

Note: DKD = 1, non-DKD = 0. Coding: educational level (middle school or below = 1, higher = 0); BMI classification (obesity = 1, overweight = 0); antihypertensive medication use (yes = 1, no = 0). The Enter method was used. Hosmer–Lemeshow $\chi^2 = 43.865$, $P < 0.01$; classification accuracy = 72.1%. CV, coefficient of glycemic variability; SBP, systolic blood pressure.

2.3 Multiplicative interaction between CV and SBP for DKD

Interaction analysis revealed a significant interaction between systolic blood pressure and coefficient of glycemic variability (interaction term $OR = 1.073$, 95%CI 1.005–1.147, $P = 0.036$). This indicated that elevated systolic blood pressure could amplify the risk effect of glycemic variability on DKD, suggesting a synergistic interaction between the two indicators (Table 3).

Table 3
Multiplicative interaction between CV and SBP for DKD

Variable	B	SE	Wald χ^2	P	OR (95% CI)
SBP	0.01	0.002	5.482	< 0.001	1.019 (1.012–1.027)
CV	2.479	0.488	25.825	< 0.001	11.926 (4.585–31.024)
SBP $\times$ CV (interaction term)	0.071	0.034	4.405	0.036	1.073 (1.005–1.147)

Note for Table 3

Note: Adjusted for educational level, BMI classification, serum uric acid, total cholesterol, and antihypertensive medication use. SBP and CV were mean-centered before constructing the interaction term. CV, coefficient of glycemic variability; SBP, systolic blood pressure.

2.4 Additive interaction between CV and SBP for DKD

Using the low CV + normal SBP group as the reference, the risk of DKD was significantly higher in individuals with high glycemic variability combined with elevated SBP ($OR = 1.649, P < 0.001$). However, the 95% confidence intervals of the additive interaction measures RERI, API, and S all crossed 0, and no statistically significant excess synergistic effect on renal injury was detected (Table 4).

Table 4
Additive interaction analysis of CV and SBP on DKD

CV group	SBP group	Total (n)	DKD cases (%)	OR (95% CI)
Low	Normal	951	371 (39.0)	1.000 (reference)
High	Normal	651	242 (37.2)	1.041 (0.820–1.323)
Low	Elevated	1025	578 (56.4)	1.257 (1.008–1.567)
High	Elevated	535	310 (57.9)	1.649 (1.276–2.131)

Note for Table 4

Note: Adjusted for total cholesterol, serum uric acid, antihypertensive medication use, educational level, and BMI classification. $SBP \geq 130$ mmHg was defined as elevated SBP. CV cutoff = 0.37. RERI = 0.351 (95% CI -0.212 to 0.914); API = 21.3% (95% CI -12.9% to 55.5%); S = 2.18. CV, coefficient of glycemic variability; SBP, systolic blood pressure; RERI, relative excess risk due to interaction; API, attributable proportion due to interaction; S, synergy index.

2.5 Results of stratified regression analysis

SBP stratification showed that CV was not significantly associated with DKD in the normal SBP group ($OR = 1.440, P = 0.520$), whereas CV was significantly associated with DKD in both the borderline SBP group ($OR = 17.089, P = 0.002$) and the hypertension group ($OR = 15.875, P = 0.007$), with the OR showing an increasing trend as SBP rose. BMI stratification showed that CV was significantly associated with DKD in both the overweight group ($OR = 22.198, P < 0.001$) and the obese group ($OR = 7.659, P = 0.002$) (Table 5).

Table 5

Stratified logistic regression analysis of the association between CV and DKD in different subgroups

Subgroup	Criteria	N (cases)	CV OR (95% CI)	P
BMI	Overweight ($24.0 \leq \text{BMI} < 28.0$ kg/m ²)	1658	22.198 (4.789–102.908)	< 0.001
BMI	Obesity ($\text{BMI} \geq 28.0$ kg/m ²)	1502	7.659 (2.140–27.415)	0.002
SBP	Normal ($\text{SBP} < 130$ mmHg)	1601	1.440 (0.475–4.362)	0.520
SBP	Borderline ($130 \leq \text{SBP} < 140$ mmHg)	844	17.089 (2.762–105.742)	0.002
SBP	Hypertension ($\text{SBP} \geq 140$ mmHg)	715	15.875 (2.162–116.546)	0.007

Note for Table 5

Note: Adjusted for total cholesterol, serum uric acid, antihypertensive medication use, and educational level. The BMI-stratified model was additionally adjusted for SBP. CV, coefficient of glycemic variability; SBP, systolic blood pressure; BMI, body mass index.

3 Discussion

The present study showed that elevated CV was an independent risk factor for DKD. Long-term variability in HbA1c has been demonstrated to be an independent risk factor for DKD, with a predictive value superior to that of a single HbA1c measurement^[9, 11]. Studies based on continuous glucose monitoring data have shown that time in range is negatively correlated with DKD severity, and elevated CV can significantly increase the risk of DKD^[12], and this conclusion has been further validated in multiple subsequent retrospective and prospective cohort studies^[13–15]. Previous studies have also shown that glycemic variability is associated with diabetic microvascular complications, and its injurious effects may be independent of mean blood glucose levels^[16]. Unlike middle-aged and elderly patients, young individuals have no long-term chronic metabolic injury in the kidney, but may be more sensitive to the acute oxidative stress caused by marked glycemic fluctuations, and short-term glycemic variability alone can induce early glomerular injury^[17]. In this study, no statistically significant difference in HbA1c was observed between the two groups, whereas the difference in CV was significant, and MBG in the DKD group was also significantly higher than that in the non-DKD group. When HbA1c did not differ, CV was still able to distinguish the two groups, suggesting that CV may provide additional information independent of mean blood glucose and may be more sensitive than static glycated hemoglobin in the early screening of DKD in young individuals.

This study found a multiplicative interaction between CV and SBP for DKD, and stratified analysis also showed that elevated SBP enhanced the risk of renal injury associated with glycemic variability. The possible mechanism is that glycemic variability damages vascular endothelium and reduces vascular

compliance through oxidative stress [5], and the two may jointly accelerate glomerulosclerosis^[18]. Toyama et al.^[19] also confirmed a synergistic effect of blood pressure and blood glucose on CKD. The present study used dynamic CV instead of static glycemic indicators, thereby extending the applicability of this conclusion to young overweight/obese populations with T2DM. The additive interaction measures did not reach statistical significance, suggesting that the two factors did not show a clear synergistic injurious effect on the absolute risk scale. Stratified analysis further suggested that CV was not significantly associated with DKD when SBP was normal, whereas the two were significantly associated when SBP was borderline elevated or hypertensive, with the OR increasing sequentially across the normal, borderline, and hypertensive groups, supporting a modifying effect of SBP on glycemic variability-related renal injury at the subgroup level. The non-significant additive interaction may stem from the limited sample size of interaction subgroups and needs further validation in prospective studies. These findings suggest that controlling glycemic variability alone or blood pressure alone is insufficient to maximally reduce the risk of DKD, and that clinical management should implement dual intervention targeting both glycemic stability and blood pressure.

The study found that obesity was an independent risk factor for DKD, consistent with the pathophysiological mechanisms by which obesity damages the kidney through multiple pathways, including the induction of insulin resistance and the promotion of inflammatory responses and oxidative stress^[18]. BMI stratification showed that the OR for CV was higher in the overweight group (22.198) than in the obese group (7.659), which may be related to the fact that patients in the obese group had multiple metabolic disturbances such as hyperlipidemia and hyperuricemia, and the contribution of other metabolic factors to renal injury was relatively increased, thereby diluting the independent effect of glycemic variability.

Low educational level was an independent risk factor for DKD, consistent with previous studies^[20]. This may indirectly increase the risk of complications by affecting health literacy, treatment adherence, and self-management ability. Patients with low educational level have poorer awareness of diabetes dietary management, medication adherence, and regular screening, which may lead to suboptimal long-term glycemic and blood pressure control and indirectly accelerate renal injury. This suggests that clinical attention should be paid specifically to health education for patients with low educational level, using plain language to strengthen awareness of dietary management, medication adherence, and regular screening. Antihypertensive drug use was an independent risk factor for DKD. This variable mainly reflects indication bias for medication use rather than drug-induced renal injury. When patients seek medical care for long-term hypertension and initiate antihypertensive treatment, their duration of hypertension and blood pressure burden may have already caused glomerular injury^[21]. Although the multivariate model adjusted for SBP, the antihypertensive drug variable may still partially capture unadjusted confounding information such as the duration and severity of hypertension. This finding suggests that patients with comorbid hypertension have a higher risk of renal injury, and early blood pressure management should be emphasized in clinical practice. The median eGFR in the DKD group was lower than that in the non-DKD group, but both groups were within the normal range, possibly indicating

that the overall study population was in the early stage of DKD, and that UACR reflects early renal injury more sensitively than eGFR. Elevated total cholesterol and serum uric acid were also independent risk factors, consistent with previous studies^[22].

This study has the following limitations. First, DKD was diagnosed based on a single inpatient UACR measurement, without repeat testing at a 3-month interval to exclude transient albuminuria; this non-differential misclassification bias would generally bias effect estimates toward the null. Future prospective studies should confirm DKD diagnosis by repeated testing at 3-month intervals as required by guidelines. Second, CV was based solely on continuous glucose monitoring data during hospitalization and could not reflect long-term glycemic variability outside the hospital. Third, potential confounders such as diet, exercise, family history, antihypertensive drug subtypes, and medication adherence were not included, and residual confounding may therefore exist^[23–26]; This single-center retrospective cross-sectional study cannot establish causal relationships; our findings should be validated in future investigations.

4 Conclusions

In summary, CV and obesity were core independent risk factors for DKD in young overweight or obese patients with T2DM. A multiplicative interaction was found between CV and SBP, without a significant additive synergistic injurious effect. Elevated SBP may amplify glycemic variability–related renal injury. Clinically, for this population, coordinated management of stable glucose control and blood pressure reduction should be implemented according to SBP stratification, with regular UACR screening and comprehensive management of multiple metabolic risk factors, to achieve early prevention and control of DKD.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Henan University of Science and Technology (approval number: 2025-0275). Informed consent was obtained from all participants. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

Clinical trial number

Not applicable.

Consent for publication

Not applicable. This manuscript does not contain any individual person's data in any form.

Availability of data and materials

The data that support the findings of this study were collected from the electronic medical record system of the hospital. Due to ethical approval and patient privacy protection, the raw data are not publicly available. De-identified analysis datasets may be made available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yang ML: Conceptualization, Methodology, Formal analysis, Writing – original draft.

Liu C: Data curation, Investigation, Methodology

Liu P: Investigation– review & editing.

Liu FF: Investigation – review & editing.

Yuan HP: Methodology– review & editing.

Gao MX: Methodology – review & editing.

Jia ZM: Supervision, Validation, Writing – review & editing.

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References

1. Teufel F, Orgutsova K, Genitsaridi I, et al. Global, regional, and national estimates of undiagnosed diabetes in adults: findings from the 2025 IDF diabetes atlas. *Diabetes Care*. 2026;49(3):490–6. 10.2337/dc25-2583.
2. Uma A, Shanmugapriyan S, Rajesh M, et al. Diabetic kidney disease in type 2 diabetes: a comprehensive review of epidemiology, pathophysiology, and therapeutic advances. *J Pharm Bioallied Sci*. 2025;17(2):33–5. 10.4103/JPBS.JPBS_1059_25.
3. Wang Y, Gu S, Xie Z, et al. Trends and Disparities in the Burden of Chronic Kidney Disease due to Type 2 Diabetes in China From 1990 to 2021: A Population–Based Study. *J Diabetes*. 2025;17(4):e70084. 10.1111/1753-0407.70084.
4. Huang L, Pan Y, Zhou K, et al. Correlation between glycemic variability and diabetic complications: a narrative review. *Int J Gen Med*. 2023;16:3083–94.
5. Hesp AC, Smits MM, van Bommel EJM, et al. Kidney hemodynamic profile and systemic vascular function in adults with type 2 diabetes: analysis of three clinical trials. *J Diabetes Complicat*. 2022;36(3):108127. 10.1016/j.jdiacomp.2022.108127.
6. Chinese Diabetes Society. Chinese guidelines for the prevention and treatment of diabetes. (2024 edition). *Chinese Journal of Diabetes Mellitus*. 2025;17(1):16–139. 10.3760/cma.j.cn115791-20241203–00705.
7. Department of Food Safety Standards, Monitoring and Assessment, National Health Commission of the People's Republic of China; National Institute for Nutrition and Health, Chinese Center for

- Disease Control and Prevention; Expert Group for the Development of Dietary Guidelines for Adults with Obesity, et al. Dietary guidelines for adults with obesity (2024 edition). *Journal of Hygiene Research* et al. 2024;53(3):347–351. 10.19813/j.cnki.weishengyanjiu.2024.03.001
8. Chinese Diabetes Society; Office for the Prevention and Treatment of Diabetes at the Primary Care Level, National Basic Public Health Service Program. National technical guidelines for the prevention and treatment of diabetic kidney disease in primary care (2023). *Chin J Intern Med*. 2023;62(12):1394–405. 10.3760/cma.j.cn112138-20231017-00223.
 9. Muthukumar A, Badawy L, Mangelis A, et al. HbA1c variability is independently associated with progression of diabetic kidney disease in an urban multi-ethnic cohort of people with type 1 diabetes. *Diabetologia*. 2024;67(9):1955–61. 10.1007/s00125-024-06197-2.
 10. Chinese Hypertension League Prevention and Treatment Guidelines Revision Committee; Hypertension Alliance (China); Hypertension Branch of China International Exchange and Promotive Association for Medical and Health Care, et al. Chinese Guidelines for the Prevention and Treatment of Hypertension (2024 Revision). *Chinese Journal of Hypertension (Chinese and English)* et al. 2024;32(7):603–700. 10.16439/j.issn.1673-7245.2024.07.002
 11. Yan Y, Kondo N, Oniki K, et al. Predictive Ability of Visit-to-Visit Variability of HbA1c Measurements for the Development of Diabetic Kidney Disease: A Retrospective Longitudinal Observational Study. *J Diabetes Res*. 2022;2022:6934188. 10.1155/2022/6934188.
 12. Zhang Q, Xiao S, Zou F, et al. Continuous glucose monitoring derived time in range and CV are associated with elevated risk of adverse kidney outcomes for patients with type 2 diabetes. *Diabetes Metab*. 2025;51(2):101616. 10.1016/j.diabet.2025.101616.
 13. Yang L, Zhou B, Deng R. Relationship between glycemic variability and renal function progression in patients with diabetic nephropathy: a retrospective cohort study. *Med (Baltim)*. 2026;105(5):e47119. 10.1097/MD.00000000000047119.
 14. Young DL, Kim J, Park S, et al. Fasting glucose variability as a risk indicator for end-stage kidney disease in patients with diabetes: a nationwide population-based study. *J Clin Med*. 2021;10(24):5948. 10.3390/jcm10245948.
 15. Tian H, Zheng X, Wang H. Isorhapontigenin ameliorates high glucose-induced podocyte and vascular endothelial cell injuries via mitigating oxidative stress and autophagy through the AMPK/Nrf2 pathway. *Int Urol Nephrol*. 2023;55(2):423–36. 10.1007/s11255-022-03325-y.
 16. Anagnostopoulou L, Liarakos LA, Stathopoulos NI, et al. Continuous glucose monitoring and microvascular complications in diabetes: bridging glycemic metrics with clinical outcomes. *Diabetes Obes Metabolism*. 2025;28(2):840–9. 10.1111/dom.70288.
 17. Sattar N, Presslie C, Rutter MK, et al. Cardiovascular and kidney risks in individuals with type 2 diabetes: contemporary understanding with greater emphasis on excess adiposity. *Diabetes Care*. 2024;47(4):531–43. 10.2337/dci23-0041.
 18. Zhu Y, Jun M, Fletcher AR, et al. Variability in HbA1c and the risk of major clinical outcomes in type 2 diabetes with chronic kidney disease: post hoc analysis from the CREDENCE trial. *Diabetes Obes*

- Metabolism. 2025;27(6):3531–5. 10.1111/dom.16363.
19. Toyama M, Satoh M, Nakayama S, et al. Combined effects of blood pressure and glucose status on the risk of chronic kidney disease. *Hypertens Res*. 2024;47(7):1831–41. 10.1038/s41440-024-01683-x.
 20. Zhang L, Feng B, Liu Z, Liu Y. Educational attainment, body mass index, and smoking as mediators in kidney disease risk: a two–step Mendelian randomization study. *Ren Fail*. 2025;47(1):2476051. 10.1080/0886022X.2025.2476051.
 21. Joshi P, Rick G, Mesinen S, et al. Antihypertensive therapy in diabetes mellitus: efficacy, safety, and metabolic impacts in type 1 and type 2 diabetes. *Cardiovasc Diabetol – Endocrinol Rep*. 2026;12(1):4. 10.1186/S40842-.
 22. Guo J, Liu C, Wang Y, et al. Dose–response association of diabetic kidney disease with routine clinical parameters in patients with type 2 diabetes mellitus: a systematic review and meta–analysis. *EClinicalMedicine*. 2024;69:102482. 10.1016/j.eclinm.2024.102482.
 23. Zhou Y, Liu Y, Wu L, et al. Causal insights into major risk factors for diabetic kidney disease: a comprehensive meta–analysis and Mendelian randomization study. *Ren Fail*. 2025;47(1):2468741. 10.1080/0886022X.2025.2468741.
 24. Tingting G, Kai Z, Qi L, et al. Healthy lifestyle behaviors, mediating biomarkers, and risk of microvascular complications among individuals with type 2 diabetes: A cohort study. *PLoS Med*. 2023;20(1):e1004135. 10.1371/journal.pmed.1004135.
 25. Kounatidis D, Vallianou NG, Stratigou T, et al. The Kidney in Obesity: Current Evidence, Perspectives and Controversies. *Curr Obes Rep*. 2024;13(4):680–702. 10.1007/s13679-024-00583-y.
 26. Alidrisi AH, Reman AK, Alhubaish SE, et al. Prevalence of chronic kidney disease and associated risk factors in patients with Type 2 Diabetes Mellitus in Basrah, Iraq: A cross–sectional study. *Diabetes Epidemiol Manage*. 2026;21:100301. 10.1016/j.deman.2026.100301.

Figures

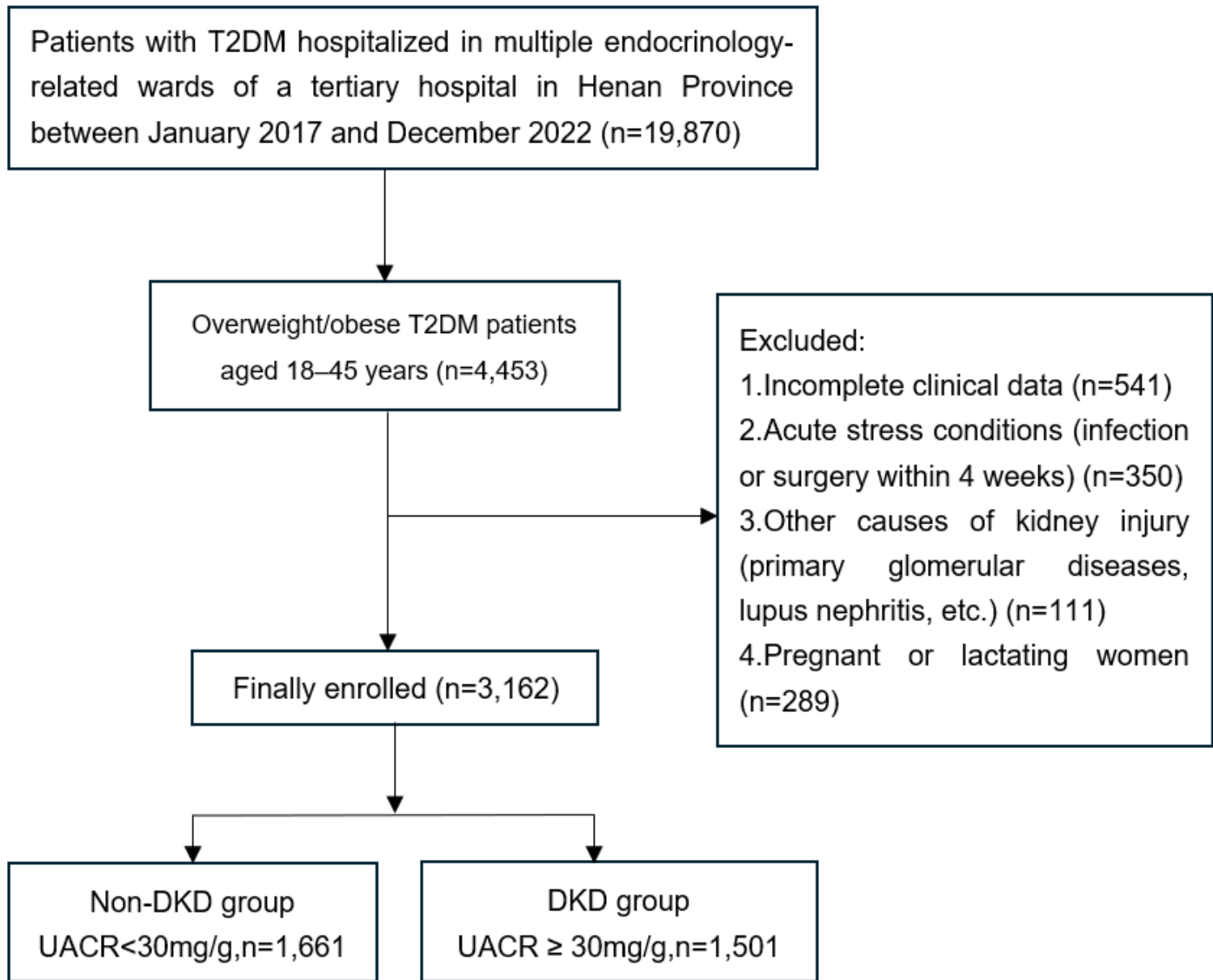


Figure 1

Flow chart of patient selection.

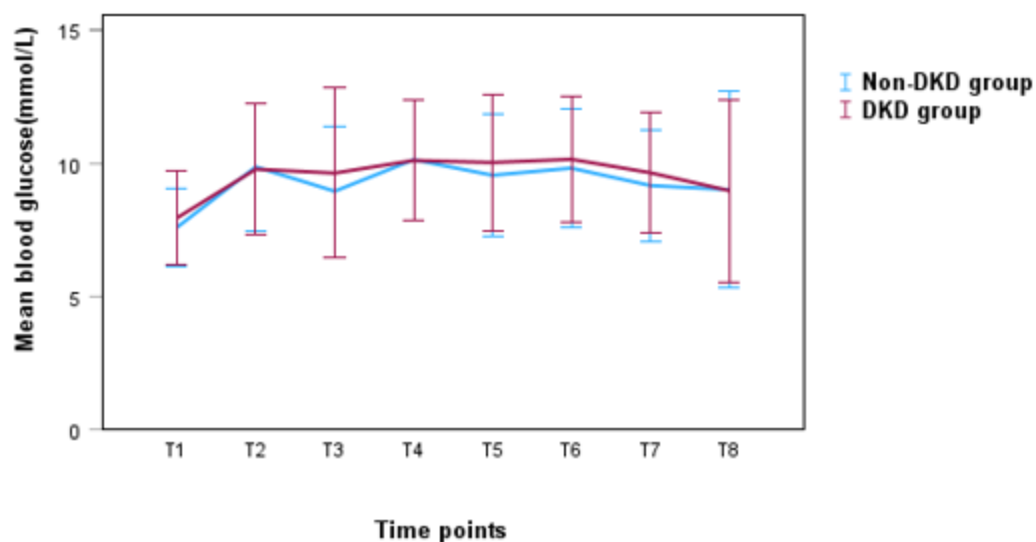


Figure 2

Comparison of mean blood glucose levels between the two groups during hospitalization.

T1–T8 indicate eight time points within a 24-hour cycle: T1, pre-breakfast; T2, 2 h post-breakfast; T3, pre-lunch; T4, 2 h post-lunch; T5, pre-dinner; T6, 2 h post-dinner; T7, bedtime; T8, 3:00 a.m. Data are expressed as mean values for each time point. Mean blood glucose concentrations at all eight time points were significantly higher in the DKD group relative to the non-DKD group (all $P < 0.05$). Error bars denote standard deviation (SD).

Supplementary Files

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- [SupplementaryTableS1.docx](#)