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Article

Risk Factor Analysis of Cardiovascular Events in Patients With Diabetic Kidney Disease and Hypertension: A Retrospective Study

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Abstract

Aims/Background: Diabetic kidney disease (DKD) is among the most prevalent complications of diabetes and is commonly accompanied by hypertension as a comorbid condition. The coexistence of these two conditions markedly augments the risk of cardiovascular disease. Although traditional risk factors such as dyslipidemia, smoking, and decreased renal function have been shown to be associated with increased cardiovascular events, evidence for the higher-risk subgroup of "DKD with hypertension" remains relatively limited. This study aimed to retrospectively analyze the influencing factors of adverse cardiovascular events in this population and assess the independent predictive value of different clinical indicators. **Methods:** In this single-center retrospective cohort study, 204 patients diagnosed with DKD and hypertension were enrolled between January 2021 and January 2024. Baseline data, including patient demographics and clinical indicators, were collected. Patients were divided into an event group and a non-event group based on whether they experienced cardiovascular events during the 12-month follow-up period. Independent risk factors were screened using univariate and multivariate logistic regression, and the effects of prior hyperlipidemia and smoking on event-free survival were assessed using Kaplan–Meier curves. **Results:** Compared with the non-event group, patients in the event group had significantly higher levels of low-density lipoprotein (LDL), urinary protein, and kidney injury molecule-1 (KIM-1), and significantly lower levels of high-density lipoprotein (HDL), along with a greater prevalence of prior hyperlipidemia and smoking (all $p < 0.05$). Univariate analysis showed that prior hyperlipidemia, smoking, elevated LDL, reduced HDL, and increased KIM-1 were all associated with cardiovascular events. Further multivariate analysis confirmed that prior hyperlipidemia, smoking, HDL, LDL, and KIM-1 were all independent predictors of cardiovascular events (all $p < 0.05$). According to Kaplan–Meier curve analysis, patients with a history of hyperlipidemia and a smoking habit had significantly lower event-free survival than those without these characteristics ($p = 0.034$ and $p = 0.024$). **Conclusion:** In DKD patients with hypertension, prior hyperlipidemia, smoking, elevated LDL, reduced HDL, and increased KIM-1 were key independent risk factors for cardiovascular events. The adverse association of dyslipidemia and smoking with event-free survival was evident early in the follow-up period. These results suggest that this high-risk population should receive enhanced lipid management and smoking cessation interventions, and the potential value of renal tubular injury markers (such as KIM-1) in cardiovascular risk assessment should be investigated to facilitate early identification of high-risk individuals and the development of individualized prevention strategies.

Keywords: diabetic kidney disease; hypertension; cardiovascular disease; dyslipidemia

1. Introduction

Diabetic kidney disease (DKD) is among the most prevalent and severe chronic complications of diabetes and represents one of the leading causes of kidney failure [1,2]. Current research indicates that approximately 20% to 40% of diabetic patients eventually develop kidney damage, and in some developed countries, nearly half of kidney failure cases originate from DKD [3]. The global prevalence of chronic kidney disease (CKD) is between 9% and 16%, and in light of the increasing annual trend of diabetes incidence, it is anticipated that the overall burden of related kidney diseases will continue to rise [4]. According to the International Diabetes Federation (IDF) Diabetes Atlas, the number of people with diabetes worldwide is projected to reach 643 million by 2030 and 783 million by 2045, placing increasing pressure on healthcare resources as the population of individuals with DKD continues to grow [5]. In terms of prognostic outcomes, DKD is associated not only with a gradual decline in kidney function but also significantly increases the risk of all-cause mortality and cardiovascular death. The mortality risk of DKD patients is approximately twice that of the general population, and their incidence of cardiovascular events is comparable to or even higher than that of those previously diagnosed with coronary artery disease [2,6]. Therefore, a growing line of evidence has corroborated DKD as a disease state with high cardiovascular risk, rather than simply a matter of kidney damage.

The pathogenesis and progression of DKD are a complex, multifactorial process involving multiple mechanisms such as metabolic imbalance, renal hemodynamic distur-

bances, activation of the renin–angiotensin–aldosterone system (RAAS), enhanced oxidative stress, immune and inflammatory activation, chronic low-grade inflammation, and impaired autophagy regulation, as well as factors such as age, genetics, and unhealthy lifestyle habits [7,8,9,10]. However, even with intensive glycemic control and aggressive antihypertensive treatment, a portion of patients still experience continued deterioration of renal function, suggesting that existing traditional risk factors cannot fully explain the pathological progression of DKD. Among the comorbidities, hypertension is one of the most common complications in DKD patients [11]. Related survey data show that 50%–80% of diabetic patients experience elevated blood pressure, and the prevalence of hypertension further increases when kidney damage occurs in diabetic patients [12]. Kidney tissue damage contributes to the RAAS activation, leading to sodium and water retention and sympathetic nervous system hyperactivity, which results in further elevation in blood pressure, thereby setting up a vicious cycle [13]. Hypertension not only exacerbates proteinuria and declining renal function but is also a significant driver of cardiovascular events in people with kidney disease. Previous studies have clearly shown that blood pressure exceeding the normal range significantly increases the risk of cardiovascular events in DKD patients and accelerates the progression to end-stage renal disease [14]. However, in actual clinical practice, there are still significant gaps in blood pressure management for patients with CKD or DKD. Some patients even have unrecognized masked hypertension or nocturnal blood pressure abnormalities, further underestimating their true cardiovascular risk.

Cardiovascular disease (CVD) has long been the leading cause of death in people with DKD, with significantly higher risk levels than those with diabetes alone or general CKD [15]. Numerous studies have shown that DKD patients have a markedly increased risk of developing coronary artery disease, stroke, and other adverse cardiovascular events, with this elevated risk approaching that observed in patients already diagnosed with coronary artery disease [16,17,18]. This risk stems not only from traditional factors such as hypertension, dyslipidemia, obesity, and smoking, but also from mechanisms such as endothelial dysfunction, inflammatory activation, and excessive oxidative stress caused by kidney damage. Therefore, early identification of factors that contribute to increased cardiovascular risk in DKD patients is crucial for guiding precise interventions. Although existing research has focused on the cardiovascular risk in DKD patients, evidence remains relatively limited for the higher-risk group, particularly DKD patients with hypertension. Existing literature suggests that factors such as proteinuria, lipid abnormalities (especially elevated triglycerides, high low-density lipoprotein [LDL] cholesterol, and low high-density lipoprotein [HDL] cholesterol), smoking, and inflammatory responses may all increase cardiovascular risk [19]. However, whether these factors still have an independent effect on DKD patients with concurrent hypertension, and whether their magnitude is affected by the interaction effects of metabolic factors, remains to be further clarified. Given our clinical observation that most DKD patients often struggle with multiple metabolic disorders, early screening of predictive variables for informing prophylactic strategies is even more valuable than treatments.

Against this backdrop, this study focuses on patients with hypertension and kidney disease. By analyzing the association between routine clinical indicators and cardiovascular events, the study aims to explore risk factors for CVD. Identifying key risk factors for cardiovascular events enables early recognition of high-risk individuals and supports more proactive interventions. This study provides new evidence to improve the early identification of cardiovascular events in DKD patients, facilitating the formulation of more precise, targeted management strategies and thereby improving long-term patient outcomes. Given the growing global burden of kidney disease, particularly when compounded by hypertension, clarifying these risk factors is crucial for optimizing prevention and control strategies and reducing cardiovascular morbidity and mortality.

2. Methods

2.1 Study Participants

In this retrospective cohort study, each patient was followed for a fixed period of 12 months from baseline (enrollment/first diagnosis date). Patient enrollment spanned from January 2021 to January 2024. Consequently, the 12-month follow-up for the last enrolled patients was concluded by January 2025. Data collection, including the acquisition of final follow-up records for all patients, was finalized in April 2025, ensuring that complete 12-month outcome data were available for the entire cohort. Therefore, survival analyses (Kaplan–Meier curves) for all patients were truncated at 12 months. The primary endpoint was the first cardiovascular event occurring within 12 months. The inclusion criteria included: (1) age $\geq$18 years; (2) meeting the diagnostic criteria for DKD and hypertension; (3) having complete relevant laboratory indicators, including renal function, proteinuria, blood lipids, blood pressure, and blood glucose; (4) having access to cardiovascular events and follow-up data during the study period. In this study, DKD was defined as the presence of diabetes mellitus along with either persistent albuminuria (urinary albumin-to-creatinine ratio $\geq$30 mg/g or proteinuria $\geq$0.15 g/24 h) and/or an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 [20]. Hypertension was defined as a seated office blood pressure $\geq$140/90 mmHg on at least two occasions or the current use of antihypertensive medication [21]. Patients were excluded if they met any of the following criteria: (1) comorbid severe heart failure, malignant tumors, or a history of major cardiovascular

or cerebrovascular events prior to study initiation; (2) presence of other primary kidney diseases or drug-related kidney damage; (3) missing key clinical data; (4) undetermined cardiovascular outcomes. A total of 204 patients were ultimately included.

Study outcomes were assessed based on previously completed follow-up records. All patients completed their baseline assessment at enrollment and were followed for 12 months. The final review and compilation of all patient outcome data were conducted in April 2025. The start date of follow-up was defined as the date of initial diagnosis of DKD with hypertension or the date of enrollment, and the endpoint was the date of the last available valid clinical record or the date of the first cardiovascular event. The primary endpoint was adverse cardiovascular events occurring during the follow-up period, including acute coronary syndrome, heart failure requiring hospitalization, and ischemic or hemorrhagic stroke. Patients were divided into the event group and the non-event group based on the occurrence of the endpoint event.

2.2 Measurement and Evaluation of Clinical Indicators

All clinical and laboratory data required for this study were extracted from the hospital's inpatient medical record system and electronic health records. Upon admission, patients' height, weight, and blood pressure were measured according to standardized procedures. Blood pressure measurements were performed in the morning after patients had rested for at least 10 minutes in bed, using an electronic blood pressure monitor (Jiangsu Yuyue Medical Equipment & Supply Co., Ltd., Danyang, China) to record systolic blood pressure (SBP) and diastolic blood pressure (DBP). Body mass index (BMI) was calculated. All laboratory indicators were tested on the morning of the second day of admission after an overnight fast of at least 8–12 hours, with venous blood samples collected for analysis. Enzymatic methods were used to determine lipid profiles, including low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG). Serum kidney injury molecule-1 (KIM-1) levels were quantified using enzyme-linked immunosorbent assay (ELISA), and all tests were performed according to the manufacturer's instructions. Renal function was assessed in terms of the eGFR, which was calculated using the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD–EPI) creatinine equation [22]. Urinary protein (PRO) levels were measured using random morning or 24-hour urine samples, and quantitative levels were assessed using routine laboratory immunoturbidimetry. A history of hyperlipidemia was determined from previous medical records, outpatient records, or long-term use of lipid-lowering medications. Additionally, the use of key cardiorenal protective medications at baseline—including statins, renin–angiotensin–aldosterone system inhibitors (RAASis), sodium-glucose cotransporter 2 inhibitors (SGLT2is), and glucagon-like peptide-1 receptor agonists (GLP-1 RAs)—was recorded based on medication reconciliation documented in the electronic health records. Family history of cardiovascular disease, smoking history, and drinking history were assessed based on patient self-report and documented medical records at admission.

2.3 Data Analysis

All data in this study were statistically analyzed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). First, the normality of continuous variables was tested using the Kolmogorov–Smirnov method to assess whether they conformed to a normal distribution. Normally distributed continuous variables were expressed as mean ± standard deviation (SD) and analyzed using independent samples *t*-tests. Non-normally distributed continuous variables were expressed as median and interquartile range [M (Q_1, Q_3)] and analyzed using Mann–Whitney *U* tests for intergroup comparisons. Categorical variables were presented as frequencies and percentages and compared using the chi-square test or Fisher's exact probability method.

To investigate risk factors for cardiovascular events, univariate logistic regression was first performed on candidate variables. Variables yielding a *p*-value of less than 0.05 in the univariate analysis were subsequently entered into a multivariate logistic regression model to identify independent risk factors while adjusting for potential confounders. Prior to model fitting, collinearity among the included variables was assessed using the variance inflation factor (VIF), with a threshold of VIF <5 indicating no significant multicollinearity. Odds ratios (ORs) along with their 95% confidence intervals (CIs) are reported. The model adhered to the event-per-variable (EPV) principle, ensuring at least 10 events per included variable to minimize overfitting.

Kaplan–Meier event-free survival curves were generated to visualize the association between key dichotomous risk factors and the timing of cardiovascular events. Stratification was performed for variables that were not only significantly associated with the endpoint in the multivariate model but also represented clinically actionable, binary risk factors. Between-group differences in survival were assessed using the log-rank test. Furthermore, univariable Cox proportional hazards regression models were applied to the same dichotomous risk factors to quantify the magnitude of their association with event timing. The resulting hazard ratios (HRs) and 95% CIs are annotated on the corresponding Kaplan–Meier plots.

All statistical tests were two-tailed, and a $p < 0.05$ was considered statistically significant.

3. Results

3.1 Comparison of Baseline Characteristics

This study included 204 patients with diabetic kidney disease and hypertension. Among them, 52 patients (25.49%) experienced cardiovascular events, and 152 patients (74.51%) did not. There were no statistically signif-

Table 1. Baseline characteristics of participants.

Variables	Non-event group (n = 152)	Event group (n = 52)	Statistic	p
Age (years)	64.61 ± 9.58	66.37 ± 7.31	$t = -1.378$	0.171
BMI (kg/m^2)	26.18 ± 3.87	26.46 ± 3.61	$t = -0.466$	0.642
SBP (mmHg)	143.84 ± 6.72	143.65 ± 7.60	$t = 0.168$	0.866
DBP (mmHg)	97.34 ± 5.02	98.27 ± 4.89	$t = -1.157$	0.249
eGFR (mL/min/1.73 m^2)	46.81 ± 7.79	45.27 ± 9.80	$t = 1.022$	0.310
HDL (mg/dL)	59.84 ± 14.10	52.51 ± 12.08	$t = 3.348$	<0.001
LDL (mg/dL), M (Q_1, Q_3)	102.33 (84.02, 119.56)	133.00 (122.60, 150.45)	$Z = -7.187$	<0.001
KIM-1 (ng/mL)	24.53 ± 12.75	30.89 ± 13.35	$t = -3.072$	0.002
TG (mg/dL), M (Q_1, Q_3)	173.47 (150.35, 200.97)	179.54 (158.45, 225.40)	$Z = -1.797$	0.072
PRO (g/24 h), M (Q_1, Q_3)	1.80 (0.89, 2.54)	2.23 (1.25, 2.79)	$Z = -2.008$	0.045
Gender, n (%)			$\chi^2 = 0.447$	0.504
Female	34 (22.37)	14 (26.92)		
Male	118 (77.63)	38 (73.08)		
Medication use				
ACEI/ARB, n (%)	53 (34.87)	20 (38.46)	$\chi^2 = 0.218$	0.641
Statins, n (%)	93 (61.18)	34 (65.38)	$\chi^2 = 0.291$	0.590
SGLT2i, n (%)	16 (10.53)	9 (17.31)	$\chi^2 = 1.657$	0.198
GLP-1 RA, n (%)	12 (7.89)	6 (11.54)	$\chi^2 = 0.267$	0.606
Previous history of hyperlipidemia, n (%)			$\chi^2 = 4.047$	0.044
No	113 (74.34)	31 (59.62)		
Yes	39 (25.66)	21 (40.38)		
Drinking, n (%)			$\chi^2 = 2.539$	0.111
No	138 (90.79)	43 (82.69)		
Yes	14 (9.21)	9 (17.31)		
Smoking, n (%)			$\chi^2 = 4.460$	0.035
No	101 (66.45)	26 (50.00)		
Yes	51 (33.55)	26 (50.00)		
Family history of cardiovascular disease, n (%)			$\chi^2 = 0.389$	0.533
No	98 (64.47)	36 (69.23)		
Yes	54 (35.53)	16 (30.77)		

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HDL, high-density lipoprotein; KIM-1, kidney injury molecule-1; LDL, low-density lipoprotein; PRO, urinary protein; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter 2 inhibitor; TG, triglycerides.

icant differences between the two groups in terms of age, BMI, SBP, DBP, eGFR, triglycerides, gender, drinking status, medication use, or family history of CVD ($p > 0.05$).

Regarding lipid profiles and kidney damage indicators, the event group had significantly lower HDL levels and significantly higher KIM-1 levels than the non-event group. Furthermore, the levels of LDL and urinary protein were significantly higher in the event group (all $p < 0.05$). The proportions of individuals with a history of hyperlipidemia (40.38% vs. 25.66%, $p = 0.044$) and of smokers (50.00% vs. 33.55%, $p = 0.035$) were significantly higher in the event group than in the non-event group. Detailed baseline characteristics are shown in Table 1.

3.2 Results of Univariate Regression Analysis

Univariate logistic regression analysis of all variables revealed that prior hyperlipidemia (OR = 1.963, 95% CI: 1.012–3.808, $p = 0.046$), smoking (OR = 1.980, 95% CI: 1.045–3.754, $p = 0.036$), LDL (OR = 1.060, 95% CI: 1.040–1.080, $p < 0.001$), HDL (OR = 0.960, 95% CI: 0.937–0.984, $p < 0.001$), and KIM-1 (OR = 1.039, 95% CI: 1.013–1.065, $p = 0.003$) were significantly associated with the occurrence of cardiovascular events (all $p < 0.05$) (Table 2).

3.3 Results of Multivariate Regression Analysis

Statistically significant variables identified from the univariate analysis were included in the multivariate logistic regression model. Collinearity diagnostics using variance inflation factor (VIF) were performed, and all VIF values were below 5, indicating no significant multicollinearity among the included variables. The results showed that: previous history of hyperlipidemia (OR = 4.170, 95% CI: 1.410–12.331, $p = 0.010$), smoking (OR = 4.616, 95% CI: 1.678–12.699, $p = 0.003$), LDL (OR = 1.100, 95%

Table 2. Univariate logistic regression analysis of the two groups of patients.

Variables	β	SE	Z	*p*	OR (95% CI)
Gender					
Female					1.000 (Reference)
Male	−0.246	0.368	−0.667	0.505	0.782 (0.380~1.610)
Previous history of hyperlipidemia					
No					1.000 (Reference)
Yes	0.674	0.338	1.994	0.046	1.963 (1.012~3.808)
Drinking					
No					1.000 (Reference)
Yes	0.724	0.462	1.569	0.117	2.063 (0.835~5.098)
Smoking					
No					1.000 (Reference)
Yes	0.683	0.326	2.094	0.036	1.980 (1.045~3.754)
Family history of cardiovascular disease					
No					1.000 (Reference)
Yes	−0.215	0.345	−0.623	0.533	0.807 (0.410~1.586)
ACEI/ARB	−0.155	0.332	−0.466	0.641	0.857 (0.447~1.642)
Statins	−0.181	0.336	−0.539	0.590	0.834 (0.432~1.611)
SGLT2i	−0.576	0.452	−1.275	0.202	0.562 (0.232~1.363)
GLP-1 RA	−0.420	0.528	−0.795	0.427	0.657 (0.233~1.850)
Age	0.022	0.018	1.207	0.227	1.022 (0.987~1.058)
BMI	0.020	0.043	0.468	0.640	1.020 (0.938~1.109)
SBP	−0.004	0.023	−0.169	0.866	0.996 (0.952~1.043)
DBP	−0.003	0.032	−0.091	0.927	0.997 (0.936~1.062)
eGFR	−0.022	0.019	−1.142	0.253	0.978 (0.941~1.016)
LDL	0.058	0.010	6.052	<0.001	1.060 (1.040~1.080)
HDL	−0.040	0.013	−3.197	<0.001	0.960 (0.937~0.984)
TG	0.009	0.005	1.895	0.058	1.009 (1.000~1.019)
KIM-1	0.038	0.013	2.949	0.003	1.039 (1.013~1.065)
PRO	0.181	0.143	1.265	0.206	1.198 (0.906~1.585)

OR, odds ratio; CI, confidence interval; SE, standard error.

CI: 1.067–1.134, $p < 0.001$), HDL (OR = 0.920, 95% CI: 0.883–0.959, $p < 0.001$), and KIM-1 (OR = 1.093, 95% CI: 1.045–1.143, $p < 0.001$) were all independent risk factors for cardiovascular events. Our findings demonstrated that elevated LDL and KIM-1 levels significantly increased event risk, while HDL showed a significant protective effect. The results of the multivariate analysis are shown in Table 3.

3.4 Forest Plot of Multivariate Logistic Regression Results

To visualize the effect sizes from the multivariate logistic regression, a forest plot was generated (Fig. 1). To allow clear visualization of both large and small effects within a single figure, the x-axis (odds ratio scale) was truncated, as indicated by the vertical red line. In the plot, the point estimates for elevated LDL and KIM-1 levels lie to the right of the null line (OR = 1), indicating increased risk, whereas higher HDL lies to the left, indicating a protective effect. The point estimates for the categorical variables (prior hyperlipidemia and smoking) extend beyond the displayed axis range to the right, reflecting substantially larger odds ratios (see Table 3 for exact values). Overall, the forest plot confirms the direction and relative magnitude of the associations identified in the regression analysis.

3.5 Kaplan–Meier Survival Analysis

To further evaluate the impact of different risk factors on the risk of cardiovascular events during the 12-month follow-up period, Kaplan–Meier event-free survival curves, stratified by history of hyperlipidemia and smoking status, were plotted, and differences between groups were compared using the log-rank test. The selection of these two stratification factors was based on three considerations: first, both univariate and multivariate analyses identified them as independent risk factors for cardiovascular events (Tables 2,3); second, their effects were the strongest in the multivariate logistic regression model; and finally, they are lifestyle and metabolic factors that can be clearly defined and are modifiable in clinical practice.

In the Kaplan–Meier plots (Figs. 2,3), the ‘Number at risk’ row shows the number of patients who were event-free at the start of each time interval. The ‘Cumulative events’

Table 3. Results of multivariate logistic regression analysis.

Variables	β	SE	Z	*p*	OR (95% CI)
Previous history of hyperlipidemia					
No					1.000 (Reference)
Yes	1.428	0.553	2.581	0.010	4.170 (1.410~12.331)
Smoking					
No					1.000 (Reference)
Yes	1.529	0.516	2.962	0.003	4.616 (1.678~12.699)
LDL	0.095	0.015	6.141	<0.001	1.100 (1.067~1.134)
HDL	−0.083	0.021	−3.955	<0.001	0.920 (0.883~0.959)
KIM-1	0.089	0.023	3.916	<0.001	1.093 (1.045~1.143)

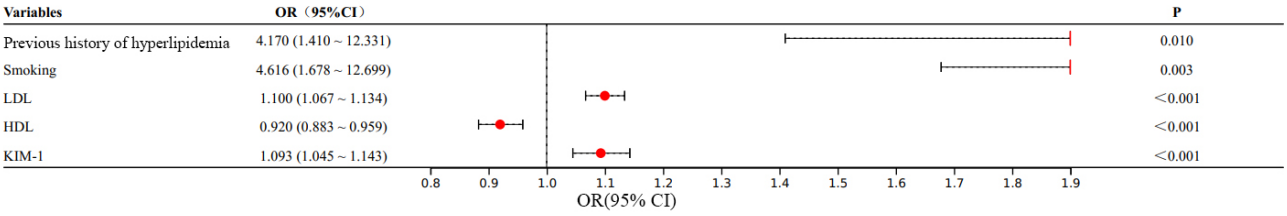

Fig. 1. Forest plot of multivariate logistic regression results. The x-axis (OR scale) was truncated at an OR of 1.9 to allow clear visualization of both large and small effects within a single figure. The point estimates for elevated LDL and KIM-1 levels are shown within the displayed range. Note that the point estimates for the categorical variables 'Prior hyperlipidemia' and 'Smoking' (indicated by the red cutoff line) lie beyond the truncated axis due to their substantially larger ORs; their exact values with confidence intervals are provided in Table 3.

row displays the total number of events that have occurred up to and including that time point. For instance, at 12 months, the cumulative number of events was 52, including 13 events identified at the final 12-month assessment visit. These 13 patients were therefore still included in the 'Number at risk' column at month 12.

Kaplan–Meier event-free survival curves based on patients' history of hyperlipidemia showed significant differences between the two groups during the follow-up period. Throughout the observation window, patients with a history of hyperlipidemia had consistently lower event-free survival rates compared to those without hyperlipidemia. Log-rank test results showed a statistically significant difference between the two groups ($p = 0.034$), confirming a significant correlation between a history of hyperlipidemia and the occurrence of cardiovascular events (Fig. 2).

Survival analysis stratified by smoking status demonstrated that the event-free survival curve in the smoking group was significantly lower than that in the non-smoking group throughout the 12-month follow-up period. Non-smokers had significantly higher event-free survival probability than smokers. The log-rank test results confirmed that this difference was statistically significant ($p = 0.024$), further indicating the adverse impact of smoking on the risk of cardiovascular events (Fig. 3).

4. Discussion

This study retrospectively analyzed the relationship between multiple clinical indicators and cardiovascular events in DKD patients with hypertension, focusing on the roles of dyslipidemia, smoking, and renal injury biomarkers in cardiovascular risk. The results showed that prior hyperlipidemia, smoking, LDL, HDL, and KIM-1 were all significantly associated with cardiovascular events, and they were identified by multivariate logistic regression as independent risk factors. Furthermore, Kaplan–Meier survival analysis further demonstrated the adverse effects of prior hyperlipidemia and smoking on event-free survival, with survival curves showing significant separation early in the follow-up period. These findings further clarify that in the high-risk population of DKD with hypertension, unhealthy lifestyle habits, metabolic abnormalities, and renal tubular damage are all strongly associated with cardiovascular risk, which may allow for more precise clinical risk identification.

The study results indicate that a history of hyperlipidemia is one of the core risk factors for cardiovascular events. This study observed a significantly higher incidence of cardiovascular events in patients with a history of hyperlipidemia, and this statistical significance remained stable in the multivariate model. This result is consistent with previous research [18]. Previous literature has confirmed that diabetic patients often exhibit a "diabetic lipid profile" characterized by high levels of triglycerides with

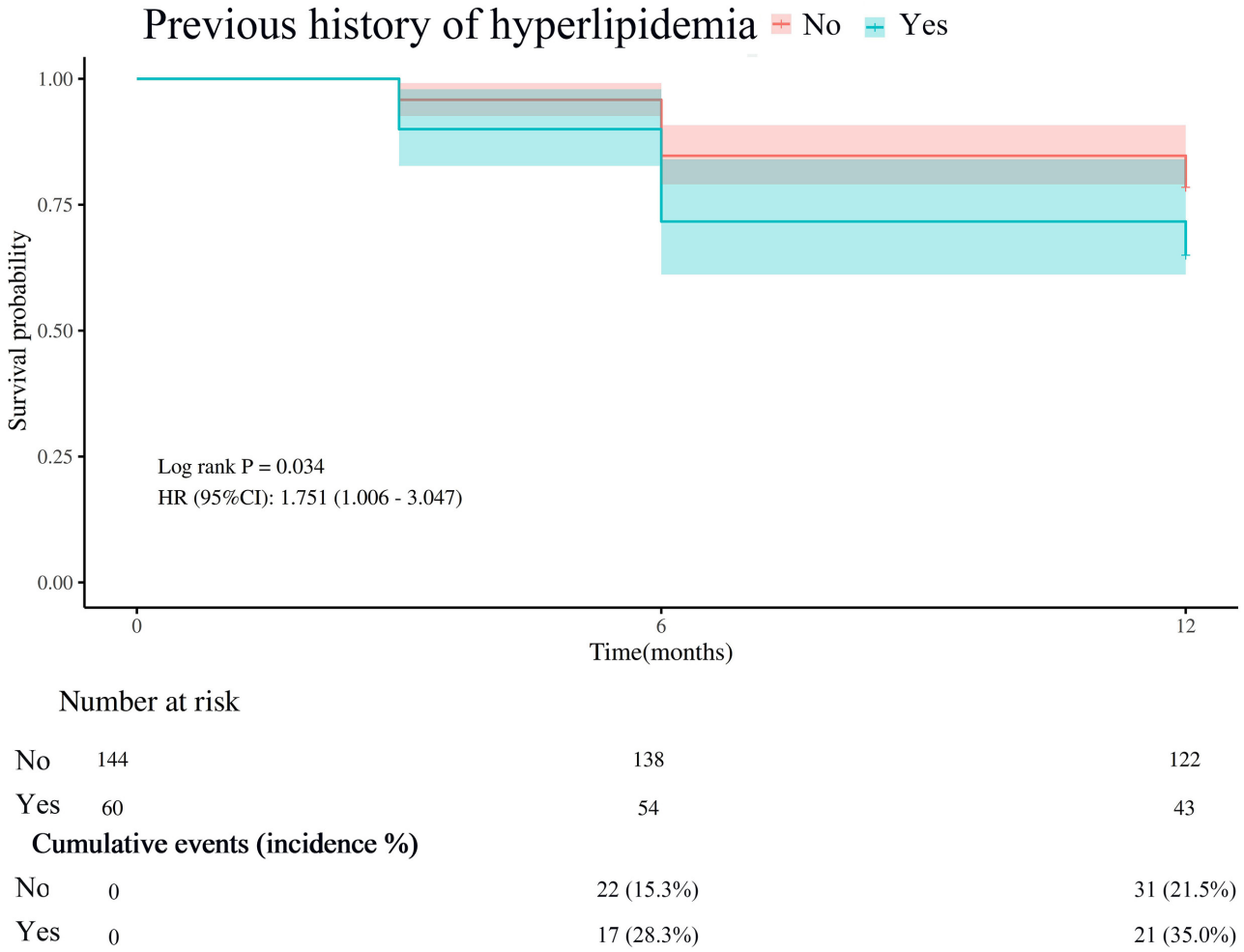

Fig. 2. Kaplan–Meier event-free survival curves for diabetic kidney disease patients with hypertension stratified by their previous history of hyperlipidemia. HR, hazard ratio.

reduced HDL. This lipid profile abnormality contributes to an accelerated progression of atherosclerosis, endothelial inflammation, and vascular stiffness, collectively augmenting cardiovascular risk [23,24]. The study by Poochanasri et al. [25] suggests that elevated LDL and decreased HDL are major risk factors for coronary heart disease and stroke in diabetic patients. Our study yielded similar conclusions regarding LDL and HDL: patients in the event group exhibited higher LDL and lower HDL, indicating that dyslipidemia is also a significant driver of cardiovascular events in individuals with DKD and hypertension. In addition to validating the predictive value of traditional lipid indicators, this study emphasizes the importance of lipid control in the context of complex metabolism. Smoking was also identified as a significant independent risk factor in this study, and its relationship with cardiovascular events was clearly demonstrated in the multivariate logistic regression results and Kaplan–Meier curves. Survival analysis showed that smokers had significantly shorter event-free survival and a 79.3% higher risk of adverse events. This association may be explained by smoking-induced oxidative stress, enhanced inflammatory responses, injury to vascular endothelium, and increased sympathetic nerve activation. In patients with DKD, smoking also contributes to and exacerbates kidney damage by reducing microvascular perfusion, aggravating proteinuria, and accelerating the decline in renal function, thereby further increasing cardiovascular risk. The results of this study are consistent with the series of reports by Yu et al. [26] and Kourtidou et al. [27], further emphasizing the impact of risk factors, such as smoking, blood lipids, HDL levels, and LDL levels, on CVD development in patients with DKD. For high-risk groups such as DKD patients with hypertension, smoking is not only a cardiovascular risk factor but also a hazardous behavior that requires rigorous intervention and management.

Notably, this study found a significant association between KIM-1 and cardiovascular events, maintaining an independent association role in a multivariate model. KIM-1, as a biomarker of renal tubular injury, reflects the degree of renal tubular epithelial cell damage, inflammation activation, and fibrosis progression. Previous studies have shown that renal tubular injury is not only related to renal prognosis

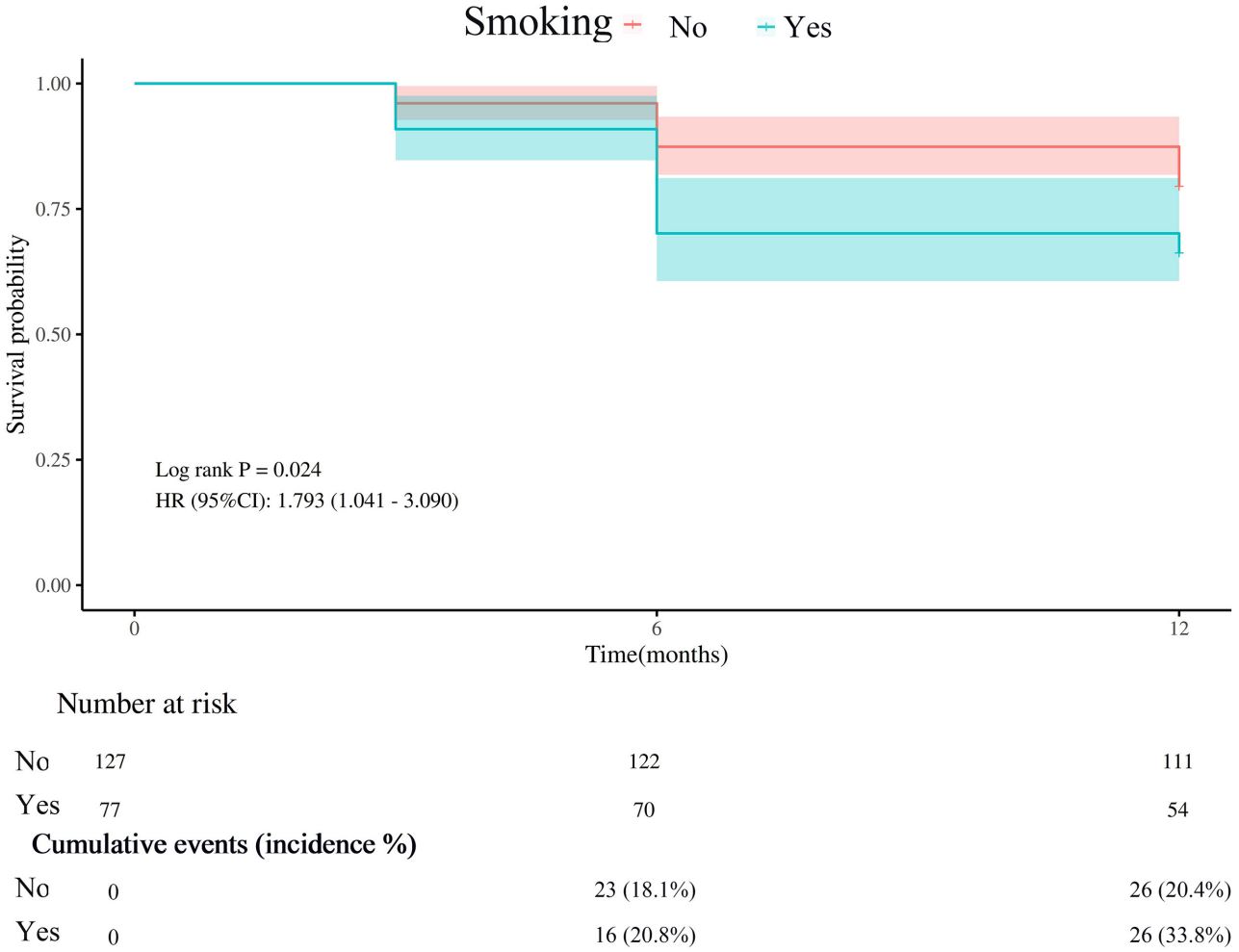

Fig. 3. Kaplan–Meier event-free survival curves for diabetic kidney disease patients with hypertension stratified by their smoking status.

but also closely linked to systemic inflammation, elevated oxidative stress levels, and endothelial dysfunction; these pathological processes stand as drivers of CVD development [28,29]. A study by Tonkonogi et al. [30] also indicated that elevated KIM-1 can predict cardiovascular events and renal endpoints in CKD patients. It should be noted that this finding is exploratory and derived from a single-center retrospective analysis. Therefore, the observed association involving KIM-1 requires validation in larger, prospective cohorts. If confirmed, KIM-1 may have potential value in identifying systemic cardiovascular risk and could be incorporated into more comprehensive risk assessment models. Based on previous literature and the results of the present study, dyslipidemia, smoking, and kidney damage are the key factors driving cardiovascular events in patients with DKD and hypertension. This retrospective study further validated the impact of these factors, which helps clinicians identify risks in the early stages of the disease and implement more targeted intervention strategies. Furthermore, the application of Kaplan–Meier survival analysis provides an intuitive depiction of the impact of high-risk factors, offering clinicians clearly defined and easily interpretable risk indicators that are useful for developing long-term follow-up strategies. The key clinical implication of the early separation in survival curves is not the exact timing of events within 12 months, but rather the clear demonstration that the excess risk associated with these factors manifests soon after clinical assessment, underscoring the need for prompt intervention.

Although this study yielded relatively reliable results, several limitations remain. First, the observational, retrospective design precludes causal inference and is susceptible to residual confounding from unmeasured or incompletely measured factors, such as socioeconomic status, dietary habits, and concurrent medication use (including duration and adherence). Second, all clinical and biomarker variables were measured only at a single time point (baseline). This precludes the assessment of their dynamic changes over the follow-up period, potentially influencing the interpretation of the cardiovascular risk and causing either underestimation or overestimation of the true effect sizes of these risk factors. Third, in this single-center

study, selection bias might exist. Fourth, with a sample size of 204 cases, the confidence intervals for some variables are relatively wide. Although the number of events met minimum modeling requirements, a larger sample would provide more stable estimates. Fifth, while key medication classes were recorded, a detailed analysis of their impact was not feasible. Future research should employ multicenter, large-sample prospective designs with serial measurements to validate these findings, better control for confounders, and elucidate temporal relationships. The exploratory association observed for KIM-1 particularly requires such prospective validation. Furthermore, the Kaplan–Meier analysis, while demonstrating early risk separation, should be interpreted with caution given the short follow-up.

5. Conclusion

This study demonstrates that in patients with DKD and hypertension, prior hyperlipidemia, smoking, elevated LDL, decreased HDL, and increased KIM-1 are all significant risk factors for cardiovascular events. Multivariate analysis demonstrated that all of these factors had independent predictive value, while Kaplan–Meier survival analysis further confirmed a significant association of hyperlipidemia and smoking with reduced event-free survival. The results suggest that, in patients with DKD and hypertension, more stringent lipid management, proactive smoking cessation interventions, and monitoring of renal tubular injury markers may help identify and manage high-risk cardiovascular subgroups. These variables may also be incorporated into a cardiovascular risk assessment system, enabling more precise and individualized management, with the ultimate goals of reducing the incidence of cardiovascular events and improving long-term patient outcomes.

Key Points

• This retrospective cohort study identified prior hyperlipidemia, smoking, elevated low-density lipoprotein (LDL), reduced high-density lipoprotein (HDL), and increased kidney injury molecule-1 (KIM-1) as independent risk factors for cardiovascular events in patients with diabetic kidney disease and hypertension.

• Kaplan–Meier analysis demonstrated that the adverse impact of hyperlipidemia and smoking on event-free survival becomes evident early, within the first year following patient assessment.

• The findings underscore the necessity for more stringent lipid management and proactive smoking cessation interventions in this high-risk population to mitigate early cardiovascular risk.

• The exploratory association between KIM-1 and cardiovascular events highlights a potential link between kidney damage and systemic risk, warranting validation in prospective studies.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

XFS and JHZ designed the research study. DQL and FJ performed the research. XFS and DQL analyzed the data. JHZ and FJ drafted this article. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of The 943 Hospital of the Joint Logistics Support Unit of the Chinese People's Liberation Army (approval number: 20251121-02), and all procedures followed the principles of the Declaration of Helsinki. As this was a retrospective study using anonymised data, the ethics committee waived the requirement for informed consent specific to this study. All patient data were kept strictly confidential.

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Conflicts of Interest

The authors declare no conflicts of interest.

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