https://nephropathol.com DOI: 10.34172/jnp.2025.27653 J Nephropathol. 2025:e27653

Journal of Nephropathology

Associated factors of kidney disease index among patients with type 2 diabetes mellitus; a cross-sectional study in Vietnam

Tuan Quoc Le[1], Khanh Minh Thanh[1], Tien Van Tran[2], Truc Quynh Doan[3], Ngan My Tang[3], Khang Minh Le Dang[4], Minh Thi Hoang[5], Tinh Thi Hoang[6], Loan Thanh Pham[7], Ha Thi Hoang Do[8], Thuan Quang Huynh[5*]

[1]Department of Physiology-Pathophysiology-Immunology, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
[2]Department of Nephrology, Ho Chi Minh City Hospital for Rehabilitation- Professional Diseases, Ho Chi Minh City, Vietnam
[3]Department of Pharmacology, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
[4]Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam
[5]Department of Biochemistry, Military Hospital 103, Vietnam
[6]Laboratory and Pathology Department, Military Institute of Traditional Medicine, Vietnam
[7]Department of Biochemistry and Microbiology, A Thai Nguyen Hospital, Vietnam
[8]Laboratory Department, Vinmec Hai Phong International Hospital, Vietnam

ARTICLE INFO

Article type:
Original Article

Article history:
Received: 23 May 2025
Revised: 16 Jul. 2025
Accepted: 8 Aug. 2025
Published online: 17 Aug. 2025

Keywords:
Kidney disease index
Estimated glomerular filtration rate
Urinary albumin-creatinine ratio
Type 2 diabetes mellitus

ABSTRACT

Introduction: The kidney disease index (KDI), a novel index combining estimated glomerular filtration rate (eGFR) and urinary albumin/creatinine ratio (UACR), has been proposed as a potential clinical tool for accurately assessing kidney function. This may aid in the better prediction of cardiovascular events in type 2 diabetes mellitus (DM) patients.

Objectives: This study aims to investigate the mean value of the KDI and to evaluate the association between KDI, clinical, and paraclinical factors, and the 10-year cardiovascular risk in type 2 diabetes patients.

Patients and Methods: A cross-sectional descriptive study was conducted on 87 individuals (42 males and 45 females) diagnosed with type 2 DM. Fasting blood samples were taken to measure fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), blood lipid profile, creatinine, and cystatin C levels. Spot urine samples were collected to assess urinary albumin, creatinine, and UACR. The eGFR values were calculated using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Creatinine-Cystatin C equation. KDI was calculated as the geometric mean of 1/eGFR and the natural logarithmic transformation of (100×UACR). Traditional cardiovascular disease risk factors were included in calculating the 10-year cardiovascular risk, based on the Framingham risk score.

Results: The results show that the mean value of KDI was 0.54±0.28. Independently associated factors with KDI were age ($P=0.044$), duration of DM ($P<0.001$), high-density lipoprotein cholesterol (HDL-c) ($P=0.008$), and HbA1c ($P=0.001$). The correlation between the 10-year cardiovascular disease risk, as determined by the Framingham risk score, and KDI (r = 0.294, $P=0.024$) was stronger than that of eGFR (r = -0.257, $P=0.049$) but not UACR (r = 0.182, $P=0.168$).

Conclusion: Adhering to recommendations for screening kidney function and injury in type 2 DM patients who are of advanced age, have a long duration of DM, have low plasma HDL-c levels, and high HbA1c levels is crucial. The potential inclusion of KDI in the prognostic models for adverse events, particularly cardiovascular disease and mortality, may provide additional insight alongside routine tests such as eGFR and UACR.

Original Article

*Corresponding author: Thuan Quang Huynh, Email: huynhquangthuan2002@yahoo.com

Implication for health policy/practice/research/medical education:
This study evaluated the kidney disease index (KDI), a new marker that combines urine albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR), among 87 patients with type 2 diabetes. The average KDI was 0.54 ± 0.28. The KDI was found to be independently associated with duration of diabetes and hemoglobin A1c (HbA1c). Additionally, KDI exhibited a stronger correlation with 10-year cardiovascular risk compared to eGFR alone.
Please cite this paper as: Le TQ, Thanh KM, Tran TV, Doan TQ, Tang NM, Dang KML, Hoang MT, Hoang TT, Pham LT, Do HTH, Huynh TQ. Associated factors of kidney disease index among patients with type 2 diabetes mellitus; a cross-sectional study in Vietnam. J Nephropathol. 2025;x(x):e27653. DOI: 10.34172/jnp.2025.27653.

Introduction

Diabetes mellitus (DM) has become a prevalent non-communicable disease, with its complications being a significant cause of morbidity and mortality worldwide. According to the 2016 Global Report on Diabetes by the World Health Organization (WHO) the number of adults diagnosed with DM rose from 108 million in 1980 to 422 million in 2014 (1). The global prevalence of DM has increased significantly, contributing to a rise in diabetic kidney disease (DKD) (2).

The harmful effects of hyperglycemia are divided into macrovascular complications (peripheral arterial disease, coronary artery disease and stroke) and microvascular complications (neuropathy, diabetic nephropathy, and retinopathy) (3). DKD associated with DM occurs in 20 to 40% of DM patients (4). In addition, DKD typically develops after a duration of 10 years in type 1 DM, with the most common onset occurring 5 to 15 years after the diagnosis; however, DKD may be present at the time of diagnosis of type 2 DM (5).

Estimated glomerular filtration rate (eGFR) and level of albuminuria, as measured through the urine albumin-to-creatinine ratio (UACR), are routinely used for individuals with DM and are important for predicting kidney outcomes, cardiovascular outcomes, all-cause mortality risks, and cardiovascular mortality risks (6). Some studies suggested that kidney disease index (KDI) may provide a more straightforward way of identifying high-risk individuals most likely to benefit from preventive therapies (7,8). Based on the results of previous studies, we assume that higher values of KDI are also positively correlated with higher cardiovascular risk.

Objectives

We conducted this study to investigate the mean value of KDI and its associations with relevant characteristics among Vietnamese patients with type 2 DM.

Patients and Methods

Study design and participants

A cross-sectional descriptive analysis study was conducted on patients with type 2 DM at the University Medical Center–Branch 2 outpatient clinic, Ho Chi Minh City, Vietnam, from December 2023 to April 2024.

Inclusion and exclusion criteria

Inclusion criteria were established for eligibility. Participants were required to have a confirmed diagnosis of type 2 DM based on the 2023 American Diabetes Association (ADA) criteria and to be actively receiving follow-up care at the clinic. Participants had to be 18 years old and provide voluntary informed consent to participate in the study.

A strict set of exclusion criteria was applied to ensure a homogeneous study population and minimize confounding factors. Patients with pre-existing hemoglobinopathies, prior diagnosed nephropathy, nephrotic syndrome, recurrent or prolonged hematuria (>3 months), or a rapid decline in eGFR (defined as a >30% increase in serum creatinine within three months) were excluded. Additionally, the study did not include individuals with kidney transplants, non-GFR-related creatinine abnormalities (due to muscle hypertrophy, bodybuilding, pregnancy, amputations, and medications affecting creatinine), non-DM-related albuminuria, or malignancies.

Data collection

Fasting blood samples (collected after an 8-12 hour overnight fast) were analyzed for fasting plasma glucose (FPG), glycated hemoglobin A1c (HbA1c), blood lipid profiles (total cholesterol, HDL-c, LDL-c and triglycerides), kidney function biomarkers (serum creatinine, serum cystatin C). eGFR values were calculated using the CKD-EPI Creatinine-Cystatin C equation (2021), which was recommended by the National Kidney Foundation and the American Society of Nephrology (9). Additionally, spot urine samples were collected to assess kidney damage via the UACR.

Fructosamine (µmol/L) concentrations measured using the Cobas 8000 colorimetric analyzer (Roche Diagnostics, Switzerland); HbA1c (%) levels determined using the Bio-Rad D-10® high-performance liquid chromatography analyzer (Bio-Rad Laboratories, USA). Serum creatinine and cystatin C were analyzed on Beckman Coulter 400 AU analyzer (Beckman Coulter, Inc., USA); serum creatinine

measured by the kinetic color test (Jaffé method) (mg/dL), calibrated to isotope dilution mass spectrometry (IDMS), and serum cystatin C measured by IDMS method (mg/L). Urinary albumin and creatinine concentrations from spot urine samples were measured using a Mission® U500 urine analyzer (ACON Laboratories, USA). All blood and urine analyses were conducted using standardized procedures in the Department of Laboratory, University Medical Center–Branch 2, Ho Chi Minh City, Vietnam.

KDI calculation

KDI was calculated as the geometric mean of 1/eGFR and natural logarithmic transformation of (100×UACR), using the following formula (8);

$$\sqrt[2]{1/\text{eGFR} \times \ln(100 \times \text{UACR})}$$

Outcomes

The Framingham risk score was used to assess the 10-year risk of cardiovascular disease in patients aged 30-74 years based on traditional cardiovascular risk factors (10). The results of traditional cardiovascular risk factors (sex, age, systolic blood pressure, anti-hypertensive treatment, current smoking, DM, HDL-c, and total cholesterol) were entered to calculate the 10-year cardiovascular risk (%) using the online calculator available at http://www.framinghamheartstudy.org/risk/coronary.html (11).

Statistical analysis

Using Microsoft Office Excel 2019 for initial data organization, data analysis was performed using SPSS 27.0 for statistical tests and visualizations. The Kolmogorov-Smirnov test was conducted to assess the normality of the data. Categorical data were presented as frequencies and percentages. Continuous variables with normal distributions were described using the mean ± standard deviation (SD), while non-normally distributed variables were summarized as the median (interquartile range). Statistical significance was set at a two-tailed *P* value of < 0.05.

A variety of statistical tests were used based on the characteristics of the data. Using chi-square or Fisher's exact test to compare proportions between groups, Student's T test or Mann-Whitney U test were employed to compare means between two groups. To evaluate the correlation between the variables, we used Pearson's or Spearman's correlation. The direction of the correlation coefficient indicated the direction of the association, with positive values representing positive relationships and negative values representing inverse relationships.

Results

Table 1 presents the clinical characteristics of the participants. Table 2 shows the reflective indicators of kidney function and damage. The median eGFR was 37.0 (23.0–50.0) mL/min/1,73 m^2, the median inverse of eGFR (1/eGFR) was 0.027 (0.02–0.04). Regarding proteinuria status, the median UACR was 245.31 (23.00–853.00) mg/mmol, and the mean ln (100×UACR) was 9.64 ± 2.16. The mean KDI in our study was 0.47 ± 0.17.

Table 1. Clinical characteristics of study participants

Characteristics	Median (IQR)
Age (years)[a]	67.33 ± 13.92
Duration of DM (years)	7.00 (3.00–13.00)
BMI (kg/m^2)	23.95 (21.93–25.51)
Triglyceride (mmol/L)	2.28 (1.60–4.52)
Total cholesterol (mmol/L)	4.40 (3.30–6.10)
LDL-c (mmol/L)	2.82 (1.90–3.60)
HDL-c (mmol/L)	0.97 (0.85–1.19)
HbA1c (%)	6.90 (6.16–8.50)
FPG (mg/dL)	131.00 (106.20–159.00)
The Framingham risk score	23.60 (16.80–30.30)

[a] Data are expressed as mean ± SD.

Abbreviations: DM, diabetes mellitus; BMI, body mass index; LDL-c, Low-density lipoprotein cholesterol; HDL-c, High-density lipoprotein cholesterol; FPG, Fasting plasma glucose.

Table 2. Characteristics of kidney disease index

Characteristics	Median (IQR)
eGFR	37.00 (23.00 – 50.00)
1/eGFR	0.03 (0.02 – 0.04)
UACR	27.72 (2.60 – 96.39)
ln (100×UACR)[a]	7.46 ± 2.16
KDI[a]	0.47 ± 0.17

[a] Data are expressed as mean ± SD.

Abbreviations: ln, Natural logarithm; KDI, kidney disease index; eGFR, estimated glomerular filtration rate; UACR, Urine albumin-to-creatinine ratio.

Using the mean value of KDI as the cutoff. Differences in clinical and paraclinical characteristics were evaluated between the two groups, KDI <0.47 and KDI ≥0.47

In our study, KDI had a significantly positive correlation with age (r = 0.274; *P* = 0.010), duration of DM (r = 0.481; *P* = 0.001), the Framingham risk score (r = 0.294; *P* = 0.024), however no significant correlation with other clinical characteristics was found. Among paraclinical values, KDI showed a statistically significant correlation with FPG (r = 0.215; *P* = 0.045), HbA1c (r = 0.288; *P* = 0.007), HDL-c (r = -0.330, *P* = 0.002) (Table 3).

Of 87 study participants, 59 (67.8%) were aged 30-74 years and eligible for the Framingham cardiovascular risk calculation. In these eligible participants, Spearman's correlation analysis evaluated the relationship between 10-year cardiovascular risk and the three factors: eGFR, UACR, and KDI (Table 3).

Kidney disease index

Conducted univariate linear regression analysis to assess whether the independent variable (KDI) could be predicted by each independent variable (age, duration of DM, HbA1c, FPG, HDL-c and the Framingham risk score) (Table 4). The multivariable linear regression analysis included all covariates with a $P < 0.25$ in the univariate linear regression analysis (age, duration of DM, HbA1c, FPG, HDL-c and the Framingham risk score).

A multivariable regression model was statistically significant ($F(6, 52) = 5.35$; $P < 0.001$) and met the assumptions required for valid linear regression. The coefficient of determination ($R^2 = 0.382$) indicates that the independent factors with KDI were duration of DM and HbA1c, accounting for 38.2 % of the variation in the KDI (Table 4).

Discussion

Our study showed that the mean age of the KDI<0.47 group (63.83 ± 12.90 years) was statistically significantly lower than that of the KDI ≥ 0.47 group (71.45 ± 14.10 years; $P = 0.008$). the study by Gerstein et al also recorded similar results, with a difference in mean age between five percentiles of the KDI ($P < 0.0001$). Meanwhile, the meta-analysis by Azagew et al combining the results of 11 previous studies enrolled patients aged ≥55 years with DKD. The analysis found an adjusted odds ratio (aOR) of 1.11 (95% confidence interval [CI] = 1.03–1.20), with a heterogeneity index (I^2) of 0.0% and a p-value of 0.488 (12). With increasing life expectancy and changes in the nutritional composition of diets, the number of patients with high-risk factors related to heart disease is rising, contributing to the increased prevalence of DKD, especially in older adults (13). The decline in renal function with age may play a role in this trend, as aging is associated with a gradual decline in GFR (14). Our study found that the decline in eGFR is more pronounced than UACR across age groups.

The male distribution between the two KDI groups (KDI <0.47 group: 53.2%; KDI ≥0.47 group: 42.5%)

Table 3. Correlation between kidney related characteristics and clinical characteristics

Characteristics		Correlation coefficient (95% CI)	*P* value
Age (years)	UACR	-0.024 (0.240 – 0.194)	0.815*
	eGFR	-0.396 (-0.564 – -0.196)	<0.001*
	KDI	0.274 (0.068 – 0.459)	0.010**
Duration of DM (years)	UACR	0.261 (0.047 – 0.452)	0.043*
	eGFR	-0.479 (-0.630 – -0.293)	<0.001*
	KDI	0.481 (0.295 – 0.632)	<0.001*
BMI (kg/m²)	UACR	-0.005 (-0.222 – 0.212)	0.962*
	eGFR	-0.031 (-0.246 – 0.187)	0.775*
	KDI	0.036 (-0.182 – 0.250)	0.742*
Triglyceride (mmol/L)	UACR	0.255 (0.041– 0.447)	0.017*
	eGFR	-0.111 (-0.320 – 0.108)	0.035*
	KDI	0.189 (-0.029 – 0.389)	0.080*
Total Cholesterol (mmol/L)	UACR	0.148 (-0.071 – 0.354)	0.148*
	eGFR	0.202 (-0.016 – 0.401)	0.061*
	KDI	-0.087 (-0.298 – -0.132)	0.422*
LDL-c (mmol/L)	UACR	0.145 (-0.074 – 0.350)	0.181*
	eGFR	0.194 (-0.024 – 0.394)	0.072*
	KDI	-0.080 (-0.292 – 0.139)	0.461*
HDL-c (mmol/L)	UACR	-0.107 (0.170 – 0.546)	0.373*
	eGFR	0.357 (0.152 – 0.546)	<0.001*
	KDI	-0.319 (-0.501 – -0.109)	0.003*
HbA1c	UACR	0.390 (0.189 – 0.559)	<0.001*
	eGFR	-0.215 (-0.413 – 0.002)	0.045*
	KDI	0.302 (0.092 – 0.487)	0.004*
FPG	UACR	0.396 (0.196 – 0.564)	<0.001*
	eGFR	-0.113 (-0.322 – 0.106)	0.298*
	KDI	0.234 (0.018 – 0.429)	0.029*
The Framingham risk score	UACR	0.182 (-0.085 – 0.425)	0.168*
	eGFR	-0.257 (-0.487 – 0.007)	0.049*
	KDI	0.294 (0.034 – 0.517)	0.024*

Abbreviation: UACR, Urine albumin to creatinine ratio; BMI, Body mass index; eGFR, estimated glomerular filtration rate; CI, Confidence interval; DM, Diabetes mellitus; UACR, Urine albumin to creatinine ratio; KDI, kidney disease index; FPG, Fasting plasma glucose; HbA1c, Glycated hemoglobin A1c; LDL-c, Low-density lipoprotein cholesterol; HDL-c, High-density lipoprotein cholesterol.

* Spearman's rank correlation analysis; ** Pearson's correlation analysis.

Table 4. Univariate linear regression analysis and multivariate linear regression model with KDI as a dependent variable

Characteristics	Unstandardized coefficients		Standardized coefficients	T	P value
	B	Standard error			
Univariate linear regression analysis					
Age (years)	0.003	0.001	0.254	2.421	0.018
Duration of DM (years)	0.012	0.002	0.480	5.042	<0.001
HDL-c (mmol/L)	-0.164	0.067	-0.256	-2.437	0.017
FPG (mg/dL)	0.00062	0.000318	0.207	1.950	0.054
HbA1c (%)	0.029	0.010	0.306	2.966	0.004
The Framingham risk score	0.006	0.003	0.264	2.069	0.043
Multivariate linear regression model					
Age (years)	0.002	0.002	0.120	0.916	0.364
Duration of DM (years)	0.008	0.003	0.319	2.718	0.009
HDL-c (mmol/L)	-0.132	0.079	-0.193	-1.683	0.098
FPG (mg/dL)	-0.0003	0.0004	-0.119	-0.826	0.413
HbA1c (%)	0.042	0.013	0.459	3.135	0.003
The Framingham risk score	0.003	0.003	0.125	0.974	0.335
Constant	0.162	0.121		1.336	0.185

Abbreviation: DM, Diabetes mellitus; HDL-c, High-density lipoprotein cholesterol; VIF, Variance inflation factor; FPG, Fasting plasma glucose; HbA1c, Glycated hemoglobin A1c.
Note: A value of VIF <2 was identified as multicollinearity is not presented.

showed no significant difference ($P = 0.320$). In contrast, Gerstein et al found differences in female distribution across the five quintiles of KDI (8). The difference in sex distributions in advanced stages of DKD may be attributed to variations in sex hormones. Estrogen may have a potential reno-protective effect (15). Estrogen has anti-inflammatory properties and regulates immune responses of cells as demonstrated by the detection of estrogen receptors on the surface of T cells and antigen-presenting cells (16). These receptor-mediated signaling can regulate immune responses and protect kidneys from hyperglycemia-induced damage. However, in postmenopausal women, as endogenous estradiol levels decreases, the reno-protective effects of anti-inflammation and regulation of immune responses are significantly reduced (17).

In our study, the median duration of DM was 7 (3.00–13.00) years. There was a significant difference in the median duration of DM between the KDI < 0.47 group and the KDI≥0.47 group ($P < 0.001$). This finding was consistent with the conclusions of a previous study by Gerstein et al, in which there was a statistically significant difference in the mean duration of DM: 9.5 ± 6.6; 9.6 ± 6.6; 10.3 ± 6.8; 10.7 ± 7.4 and 12.5 ± 8.2 years from the first to the fifth quartile ($P < 0.0001$) (8). Likewise, Azagew et al examined 10 previous studies. They found that diabetic patients with a longer duration of DM (≥10 years) were 1.23 times more likely to develop DKD compared to those with a shorter duration (aOR = 1.23; 95% CI = 1.05–1.45; heterogeneity index I2 = 0.0%, p = 0.567) (12). A study involving 11,140 type 2 DM patients by Zoungas et al reported that duration of DM was independently associated with microvascular events (hazard ratio [HR] = 1.28; 95% CI = 1.23–1.33), and for every 5 years of duration of type 2 DM, the risk of microvascular events increased by 28% (18). The duration of type 2 DM is a crucial factor in developing DKD. Therefore, intensive and appropriate care for DM patients, particularly the elderly, may slow the progression of long-term complications and improve quality of life.

In our study, we did not find a statistically significant difference in median systolic blood pressure ($P = 0.939$) or diastolic blood pressure (p = 0.156) between the two groups of KDI. The study by Gerstein et al reported a statistically significant difference in mean systolic blood pressure ($P < 0.0001$), but not diastolic blood pressure ($P = 0.3296$) across five quartiles of KDI (8). There is a change in blood pressure according to the diurnal rhythm in the group of DM patients with hypertension (19). It is possible that study participants in the KDI group ≥0.47 include individuals with non-dipper blood pressure (no decrease or little decrease blood pressure at night) and people with reverse dipper (blood pressure at night is higher than during the day), and these two forms of increased blood pressure are related to cardiovascular risk (20). Therefore, ambulatory blood pressure monitoring in DM patients with hypertension should be performed to identify this hidden uncontrolled hypertension (21). Besides, study

participants might have well-controlled blood pressure due to anti-hypertensive medications. The goal of optimal blood pressure control in patients with DKD is to reduce renal function decline and improve cardiovascular outcomes. However, the optimal blood pressure level in these patients has not yet been determined. KDIGO 2021 treatment guidelines recommend aggressive blood pressure control, with a target blood pressure level of <120 mm Hg, based on evidence that the cardiovascular benefits outweigh the risks of kidney damage associated with lower blood pressure targets (22). Nevertheless, individualized blood pressure targets may be necessary, depending on age, type of diabetes, and stage of chronic kidney disease. Less aggressive treatment strategies may be considered for older, frail patients with kidney disease but without albuminuria, due to the J-shaped relationship between lower blood pressure and cardiovascular mortality.

Our study shows that the median FPG and HbA1c between the two KDI groups are not statistically different ($P > 0.05$). In contrast, the survey by Gerstein et al showed a statistically significant difference in mean HbA1c across five quartiles of KDI ($P < 0.0001$). ADA and the European Association for the Study of Diabetes also note that HbA1c may not be reliable in advanced CKD due to its limitations in conditions that alter the erythrocyte lifespan, such as anemia, exogenous erythropoietin treatment, and other comorbidities commonly seen in this patient group (23).

Among the four types of plasma lipids, our study found statistically significant differences in the median plasma cholesterol ($P = 0.006$), HDL-c ($P = 0.014$), and LDL-c ($P = 0.008$) between the two groups of KDI. Median HDL-c levels in the group with KDI < 0.47 were significantly higher than in the group with KDI ≥0.47. Interestingly, significantly higher median plasma cholesterol and LDL-C levels were observed in the group with KDI <0.47 compared to the group with KDI ≥0.47. Gerstein et al showed a statistically significant difference in mean LDL-C levels across five quartiles (p<0.001) (8). Dyslipidemia is common and affects approximately 70–85% of patients with type 2 DM. It may be attributed to a diet high in carbohydrates and fats, low in vegetables and fruits, lack of physical activity, socioeconomic factors, and medical conditions. In type 2 DM, insulin resistance and hyperglycemia increase triglyceride levels, elevating glycerol-rich lipoproteins. A study of Xiang et al found no linear association between LDL-c levels and the risk of DKD in patients with type 2 diabetes. LDL-c levels <2.97 mmol/L may increase the risk of DKD (24). Wang et al (20) showed a U-shaped association between HDL-c levels and DKD risk in patients with type 2 DM, where both low or high HDL-c levels may increase the DKD risk in patients with type 2 DM (25).

A univariate regression analysis was conducted on variables that showed statistically significant correlations with KDI, including age, duration of DM, HDL-c, HbA1c, FPG and the Framingham risk score. Results from the univariate regression model revealed that two variables, duration of DM (p = 0.009) and HbA1c (p = 0.003), were associated with KDI but not age (p = 0.364), HDL-c (p = 0.098), FPG (p = 0.413) and the Framingham risk score (p = 0,335). The selection of potential variables (p<0.25) from univariate regression analysis was maintained for integration into the multivariate regression model. The multivariate analysis results indicated four independent associated factors with KDI were duration of DM (p = 0.009) and HbA1c (p = 0.003).

This result is consistent with findings from earlier research. DKD was associated with advanced age, longer duration of DM, poor plasma glucose control, and dyslipidemia (26). Farah et al conducted a study that utilized logistic regression analysis to examine the association of DKD and independent variables such as age >60 years, duration of DM, HbA1c >7%, demonstrating a significant association (p< 0.0001) (27). Multivariate analysis identified age >60 years (OR = 1.02; 95% CI = 1.01 –1.03; p<0.01) and low HDL-c (OR = 0.98; 95% CI = 0.97–0.99; p<0.01) as independent associated factors with DKD in DM patients (27). Another study by Duan et al presented findings from a logistic regression analysis, in which the dependent variable was the presence of DKD, revealing a positive association between DKD and advancing age (OR = 1.23; 95% CI = 1.13–1.33), dyslipidemia (OR = 2.51; 95% CI = 2.15–2.92) (28).

After examining the correlation between eGFR, UACR, and KDI with clinical and paraclinical characteristics, our findings indicated that KDI exhibited higher correlation coefficients with traditional cardiovascular disease risk factors than eGFR and UACR. We further evaluated the correlations between 10-year cardiovascular risk based on the Framingham risk score and the independent variables such as eGFR, UACR, and KDI. The findings revealed a correlation between the 10-year cardiovascular risk and KDI (r=0.294, p=0.024) that is stronger than eGFR (r=-0.257, p=0.049) but not UACR (r=0.182, p=0.168). Previous research has assessed the potential improvement in cardiovascular mortality prediction by incorporating eGFR and/or UACR into predictive models. Matsushita et al demonstrated that the inclusion of both eGFR and proteinuria in the SCORE2-OP (Systematic Coronary Risk Evaluation 2-Older Persons) models enhanced the predictive accuracy of cardiovascular disease compared to the original models by the European Society of Cardiology in 2021 (29). According to the research by Nerpin et al (30). The addition of eGFR and UACR to the traditional cardiovascular risk factors in the multivariable Cox

regression model led to enhanced accuracy in predicting cardiovascular mortality.

Conclusion

Research on the KDI, which combines two routine values (UACR and eGFR) in patients with DKD, revealed a mean KDI of 0.47 ± 0.17. Consequently, it is crucial to adhere to recommendations for screening kidney function and injury in type 2 DM patients with long duration of DM and high HbA1c. Including KDI in prognostic models for adverse events, particularly cardiovascular disease, and cardiovascular mortality, may provide additional insight beyond standard tests such as eGFR and UACR.

Limitations of the study

The cross-sectional design does not assess a causal relationship between KDI and cardiovascular risk or progression of kidney disease. Single-center collection and small sample size may limit the generalizability of the results.

Author' contribution

Conceptualization: Khanh Minh Thanh, Tuan Quoc Le.
Data curation: Tuan Quoc Le, Tien Van Tran, Truc Quynh Doan, Khanh Minh Thanh, Ngan My Tang, Khang Minh Le Dang.
Formal analysis: Tuan Quoc Le, Tien Van Tran, Khanh Minh Thanh.
Funding acquisition: Tuan Quoc Le, Khanh Minh Thanh, Tien Van Tran.
Investigation: Tuan Quoc Le, Khanh Minh Thanh,
Methodology: Tuan Quoc Le, Khanh Minh Thanh, Tien Van Tran, Truc Quynh Doan, Ngan My Tang, Khang Minh Le Dang.
Project administration: Tuan Quoc Le, Minh Hoang Thi, Thuan Huynh Quang.
Resources: Tuan Quoc Le, Khanh Minh Thanh, Truc Quynh Doan, Tien Van Tran, Ngan My Tang, Khang Minh Le Dang
Software: Tuan Quoc Le, Thuan Huynh Quang, Minh Hoang Thi.
Supervision: Tuan Quoc Le, Ngan My Tang, Khanh Minh Thanh
Validation: Tuan Quoc Le, Khanh Minh Thanh, Ngan My Tang.
Visualization: Tuan Quoc Le, Minh Hoang Thi, Thuan Huynh Quang
Writing–original draft: Tuan Quoc Le, Minh Hoang Thi.
Writing–review & editing: Thuan Huynh Quang, Tuan Quoc Le, Minh Hoang Thi.

Acknowledgments

We thank all patients for their participation in this study, the University of Medicine and Pharmacy at Ho Chi Minh City for its support, and the University Medical Center-Branch 2 for creating favorable conditions for the research to be conducted.

Conflicts of interest

The authors declare that they have no competing interests.

Data availability statement

The datasets of the current study are available from the corresponding author upon reasonable request.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Medicine and Pharmacy at Ho Chi Minh City (NO#1172/HĐĐĐ-ĐHYD; Date: November 23, 2023). Prior to any intervention, all participants provided written informed consent. The authors have fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

Funding/Support

None

References

1. WHO. Global report on diabetes. Geneva: World Health Organization; 2016.
2. Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. JAMA. 2011;305:2532-9. doi: 10.1001/jama.2011.861.
3. Fowler M. Microvascular and Macrovascular Complications of Diabetes. Clinical Diabetes. 2008;26:77-82. doi: 10.2337/diaclin.26.2.77.
4. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2023. Diabetes Care. 2023;46:S191-S202. doi: 10.2337/dc23-S011.
5. Johansen KL, Chertow GM, Foley RN, Gilbertson DT, Herzog CA, Ishani A, et al. US Renal Data System 2020 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2021;77:A7-A8. doi: 10.1053/j.ajkd.2021.01.002.
6. van der Velde M, Matsushita K, Coresh J, Astor BC, Woodward M, Levey A, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. Kidney Int. 2011;79:1341-52. doi: 10.1038/ki.2010.536.
7. Fang S, Chen Y, Gao Q, Wei Q. Association of kidney disease index with all-cause and cardiovascular mortality among individuals with hypertension. Clin Cardiol. 2023;46:1442-1449. doi: 10.1002/clc.24131.
8. Gerstein HC, Ramasundarahettige C, Avezum A, Basile J,

Conget I, Cushman WC, et al. A novel kidney disease index reflecting both the albumin-to-creatinine ratio and estimated glomerular filtration rate, predicted cardiovascular and kidney outcomes in type 2 diabetes. Cardiovasc Diabetol. 2022;21:158. doi: 10.1186/s12933-022-01594-6.
9. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al; Chronic Kidney Disease Epidemiology Collaboration. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. N Engl J Med. 2021;385:1737-1749. doi: 10.1056/NEJMoa2102953.
10. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117:743-53. doi: 10.1161/CIRCULATIONAHA.107.699579.
11. Framingham Heart Study. Cardiovascular Disease (10-year risk) 2008. 07/10/2024. Available from: https://www.framinghamheartstudy.org/fhs-risk-functions/cardiovascular-disease-10-year-risk/.
12. Azagew AW, Beko ZW, Mekonnen CK. Determinants of diabetic nephropathy among diabetic patients in Ethiopia: Systematic review and meta-analysis. PLoS One. 2024;19:e0297082. doi: 10.1371/journal.pone.0297082.
13. LeRoith D, Biessels GJ, Braithwaite SS, Casanueva FF, Draznin B, Halter JB, et al. Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2019;104:1520-1574. doi: 10.1210/jc.2019-00198.
14. Hemmelgarn BR, Zhang J, Manns BJ, Tonelli M, Larsen E, Ghali WA, et al. Progression of kidney dysfunction in the community-dwelling elderly. Kidney Int. 2006;69:2155-61. doi: 10.1038/sj.ki.5000270.
15. Valdivielso JM, Jacobs-Cachá C, Soler MJ. Sex hormones and their influence on chronic kidney disease. Curr Opin Nephrol Hypertens. 2019;28:1-9. doi: 10.1097/MNH.0000000000000463.
16. Kovats S. Estrogen receptors regulate innate immune cells and signaling pathways. Cell Immunol. 2015;294:63-9. doi: 10.1016/j.cellimm.2015.01.018.
17. Zoungas S, Woodward M, Li Q, Cooper ME, Hamet P, Harrap S, et al; ADVANCE Collaborative group. Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes. Diabetologia. 2014;57:2465-74. doi: 10.1007/s00125-014-3369-7.
18. Zoungas S, Woodward M, Li Q, Cooper ME, Hamet P, Harrap S, et al. Impact of age, age at diagnosis and duration of diabetes on the risk of macrovascular and microvascular complications and death in type 2 diabetes. Diabetologia. 2014;57:2465-74. doi: 10.1007/s00125-014-3369-7.
19. Gorostidi M, de la Sierra A, González-Albarrán O, Segura J, de la Cruz JJ, Vinyoles E, et al; Spanish Society of Hypertension ABPM Registry investigators. Abnormalities in ambulatory blood pressure monitoring in hypertensive patients with diabetes. Hypertens Res. 2011;34:1185-9. doi: 10.1038/hr.2011.100.
20. Verdecchia P, Angeli F, Mazzotta G, Garofoli M, Ramundo E, Gentile G, et al. Day-night dip and early-morning surge in blood pressure in hypertension: prognostic implications. Hypertension. 2012;60:34-42. doi: 10.1161/HYPERTENSIONAHA.112.191858.
21. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39:3021-3104. doi: 10.1093/eurheartj/ehy339.
22. Jung HH. Hypertension Management in Patients with Chronic Kidney Disease in the Post-SPRINT Era. Electrolyte Blood Press. 2021;19:19-28. doi: 10.5049/EBP.2021.19.2.19.
23. Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2022;45:2753-2786. doi: 10.2337/dci22-0034.
24. Xiang X, Chen G, Ma Y, Wang H. A non-linear association between low-density lipoprotein cholesterol and the risk of diabetic kidney disease in patients with type 2 diabetes in China. Prev Med Rep. 2024;45:102840. doi: 10.1016/j.pmedr.2024.102840.
25. Wang H, Wu J, Lin M, Hu Y, Ma Y. High levels of high-density lipoprotein cholesterol may increase the risk of diabetic kidney disease in patients with type 2 diabetes. Sci Rep. 2024;14:15362. doi: 10.1038/s41598-024-66548-2.
26. Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. Clin J Am Soc Nephrol. 2017;12:2032-2045.doi:10.2215/CJN.11491116.
27. Farah RI, Al-Sabbagh MQ, Momani MS, Albtoosh A, Arabiat M, Abdulraheem AM, et al. Diabetic kidney disease in patients with type 2 diabetes mellitus: a cross-sectional study. BMC Nephrol. 2021;22:223. doi: 10.1186/s12882-021-02429-4.
28. Duan J, Wang C, Liu D, Qiao Y, Pan S, Jiang D, et al. Prevalence and risk factors of chronic kidney disease and diabetic kidney disease in Chinese rural residents: a cross-sectional survey. Sci Rep. 2019;9:10408. doi: 10.1038/s41598-019-46857-7.
29. Matsushita K, Kaptoge S, Hageman SHJ, Sang Y, Ballew SH, Grams ME, et al. Including measures of chronic kidney disease to improve cardiovascular risk prediction by SCORE2 and SCORE2-OP. Eur J Prev Cardiol. 2023;30:8-16. doi: 10.1093/eurjpc/zwac176.
30. Nerpin E, Ingelsson E, Risérus U, Sundström J, Larsson A, Jobs E, et al. The combined contribution of albuminuria and glomerular filtration rate to the prediction of cardiovascular mortality in elderly men. Nephrol Dial Transplant. 2011;26:2820-7. doi: 10.1093/ndt/gfq848.