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The unique association between estimated pulse wave velocity and the prevalence of diabetic kidney disease: a cross-sectional study

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Abstract

Objective Arteriosclerosis plays a significant role as one of the key pathological mechanisms underlying Diabetic Kidney Disease (DKD). The estimated Pulse Wave Velocity (ePWV) is used to assess arteriosclerosis, and is considered a potential clinical surrogate for pulse wave velocity. There are no studies on ePWV in relation to DKD. Our research represents the first embark to explore the relationship between ePWV and DKD.

Methods In this cross-sectional analysis, we collected ePWV data from a cohort of 4,296 hospitalized Chinese patients. Multivariable-adjusted logistic regression models and restricted cubic spline (RCS) analysis were employed to examine the relationship between eGDR and the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2.

Results After adjusting for confounding factors, each unit increase in ePWV was associated with a 23%, 21% and 25% increase in the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2 in T2DM participants, respectively. A J-shaped relationship was observed between ePWV and the prevalence of DKD and eGFR < 60 mL/min per 1.73 m^2, and a linear association between ePWV and the prevalence of UACR ≥ 30 mg/g.

Conclusion ePWV is independently positively correlated with the prevalence of DKD. Integrating ePWV into routine clinical evaluations enable timely interventions and personalized management approaches.

Keywords Estimated pulse wave velocity, Type 2 diabetes mellitus, Diabetic kidney disease, Urinary albumin-to-creatinine ratio, Estimated glomerular filtration rate

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Introduction

Diabetes mellitus (DM) has emerged as a significant public health concern in the 21st century. Projections suggest that by 2045, there will be 783.2 million diabetic patients globally. In China alone, the diabetic population has reached 116 million, making it the highest in the world, with type 2 diabetes mellitus(T2DM) accounting for 90% of cases [1]. Among the various complications of T2DM, Diabetic kidney disease (DKD) stands out as one of the most prevalent microvascular complications. It has become a leading cause of end-stage renal disease worldwide, significantly elevating the risk of premature mortality in affected individuals, with an incidence rate of 30 – 40% among T2DM patients [2]. Hence, effectively predicting and mitigating renal function impairment in the early stages of T2DM constitutes a critical strategy in preventing the onset and progression of DKD.

Arteriosclerosis serves as the pathological cornerstone of systemic vascular ailments, particularly in cases involving T2DM, wherein its implications are intimately intertwined with the onset and progression of DKD [3–5]. Elevated arterial stiffness contributes to heightened blood flow and pulse pressure, disseminating to organs characterized by high blood flow and microvascular resistance, such as the kidneys [6]. This phenomenon can inflict damage upon the glomerulus, consequently precipitating a decline in renal function. Arteriosclerosis significantly accelerates the progression of diabetic kidney disease, exacerbating renal impairment and leading to adverse outcomes [7]. Studies have demonstrated that within the DKD patient cohort, augmented arteriosclerosis scores correlated with deteriorating renal function, consequently abbreviating the time interval progressing to end-stage renal disease [8].

Carotid-femoral pulse wave velocity (CfPWV) stands as the gold standard in clinically assessing arteriosclerosis. However, its practical application is hindered by various factors such as equipment limitations, costly testing, and complex operation [9]. Recently, estimated pulse wave velocity (ePWV) was unveiled that utilizes chronological age and blood pressure as input values to estimate the pulse wave propagation velocity. This innovation not only provides convenient results but also shows strong correlation with CfPWV outcomes [10, 11]. While ePWV cannot fully replace CfPWV, the ePWV calculation incorporates complex interactions between blood pressure and age that are not considered in traditional risk scores and are also not entirely captured by CfPWV [12]. For example, ePWV has shown promising potential in predicting cardiovascular events after adjustments based on CfPWV [13]. Additionally, although brachial-ankle pulse wave velocity (baPWV) is also considered a good marker for arterial stiffness, studies have demonstrated that ePWV outperforms baPWV in predicting cardiovascular and all-cause mortality, particularly in hypertensive patients [14]. Furthermore, ePWV has been linked to both diabetes and kidney disease [15, 16], showing potential in predicting newly diagnosed diabetes and serving as a valuable indicator for assessing mortality risk in patients with acute kidney injury. Our research represents the first embark to explore the relationship between ePWV and DKD.

Materials and methods

Study design and participants

The study enrolled a total of 6,306 individuals aged 18 and older diagnosed with T2DM, who were admitted to Guang'anmen Hospital between February 2017 and February 2022. Those with incomplete clinical data, totaling 2,010 participants, were excluded from the analysis. As a result, 4,296 participants were ultimately included in the study. This retrospective study was approved by the Medical Ethics Committee of Guang'anmen Hospital, which is affiliated with the China Academy of Chinese Medical Sciences (Approval No. 2023-187-KY). The study was carried out in strict compliance with the ethical standards set forth in the Declaration of Helsinki.

Measurements

Demographic details, blood pressure records, and clinical indices for inpatients were systematically extracted from electronic medical records by uniformly trained personnel. The ePWV was calculated using a formula first introduced by Greve et al. and further elaborated by the Arterial Stiffness Collaboration [10, 17]. The calculation is as follows: $ePWV = 9.587—0.402 \times age + 4.560 \times 10^{-2} \times age^2 —2.621 \times 10^{-5} \times age^2 \times$ Mean Blood Pressure (MBP) $+ 3.176 \times 10^{-3} \times age \times MBP— 1.832 \times 10^{-2} \times MBP$, with age measured in years and MBP derived as diastolic blood pressure (DBP) + 0.4 × (systolic blood pressure (SBP) - DBP). The estimated glomerular filtration rate (eGFR) was assessed using the Chronic Kidney Disease Epidemiology Collaboration equation, specifically designed for the Asian demographic. DKD was identified based on a Urine albumin to creatinine ratio (UACR) of ≥ 30 mg/g and/or an eGFR of < 60 mL/min per 1.73 m^2, adhering to the guidelines established by the American Diabetes Association [18].

Statistical analysis

The analysis was conducted using R (v4.4.1) and GraphPad Prism (v8.0.2), with statistical significance defined as a two-sided P-value of < 0.05. Continuous variables were presented as means ± standard deviations or medians with interquartile ranges, while categorical variables were reported as counts (percentages). ePWV was categorized into quartiles, and for trend analysis, the median value of each quartile was treated as a continuous variable in the

Table 1 General and sociodemographic characteristics of the participants by DKD

Characteristics	Non-DKD	DKD	Total	P_{value}
N	2821	1475	4296	
Age, years	59.0 [65.0–51.0]	61.0 [69.0–53.0]	59.0 [66.0–52.0]	< 0.001
Men, %	1525 (54.1%)	873 (59.2%)	2398 (55.8%)	0.001
Duration of diabetes, years	14.0 [19.0–8.00]	15.0 [21.0–9.00]	14.0 [20.0–8.00]	< 0.001
SBP, mmHg	136 [145–126]	139 [148–128]	137 [147–126]	< 0.001
DBP, mmHg	80.0 [87.0–73.0]	80.0 [88.0–73.0]	80.0 [87.0–73.0]	0.644
HbA1c, %	8.40 [9.80–7.30]	8.80 [10.2–7.50]	8.60 [10.0–7.30]	< 0.001
TC, mmol/L	4.62 [5.43–3.87]	4.73 [5.71–3.90]	4.65 [5.50–3.88]	0.002
TG, mmol/L	1.45 [2.06–1.05]	1.77 [2.56–1.22]	1.54 [2.23–1.11]	< 0.001
HDL, mmol/L	1.12 [1.31–0.960]	1.09 [1.28–0.940]	1.11 [1.30–0.950]	< 0.001
LDL, mmol/L	2.93 [3.54–2.37]	3.01 [3.69–2.38]	2.96 [3.60–2.37]	0.011
UACR, mg/g	8.63 [13.7–5.60]	102 [378–42.6]	13.1 [45.9–6.82]	< 0.001
eGFR, mL/min per 1.73 m^2	104 [114–93.9]	88.4 [107–58.3]	101 [112–85.5]	< 0.001
ePWV, m/s	10.6 [11.8–9.35]	11.0 [12.5–9.68]	10.7 [12.0–9.48]	< 0.001

DKD Diabetic kidney disease, SBP Systolic blood pressure, DBP Diastolic blood pressure, TC Total cholesterol, TG Triglycerides, HDL High-density lipoprotein, LDL Low-density lipoprotein, UACR Urine albumin to creatinine ratio, eGFR Estimated glomerular infiltration rate, ePWV Estimated pulse-wave velocity

Table 2 General and sociodemographic characteristics of the participants by ePWV quartiles

Characteristics	Quartile 1(≤ 9.48)	Quartile 2(> 9.48, ≤ 10.69)	Quartile 3(> 10.69,≤12.03)	Quartile 4(> 12.03)	$P_{for\ trend}$
N	1075(25%)	1069(24.8%)	1079(25.1%)	1073(24.9%)	
Age, years	45.0 [51.0–38.0]	56.0 [60.0–53.0]	63.0 [66.0–59.0]	71.0 [76.0–67.0]	< 0.001
Men, %	753(70.0%)	634(59.3%)	559(51.8%)	452(42.1%)	< 0.001
Duration of diabetes, years	11.0 [17.0–6.00]	14.0 [19.0–8.00]	15.0 [21.0–9.00]	16.0 [22.0–10.0]	< 0.001
SBP, mmHg	126 [136 – 119]	133 [141 – 125]	140 [148 – 131]	147 [159 – 138]	< 0.001
DBP, mmHg	79.0 [85.0–72.0]	80.0 [86.0–73.0]	81.0 [87.0–74.0]	82.0 [89.0–75.0]	< 0.001
HbA1c, %	8.90 [10.4–7.50]	8.60 [9.90–7.30]	8.40 [9.90–7.30]	8.40 [9.80–7.20]	< 0.001
TC, mmol/L	4.90 [5.72–4.16]	4.72 [5.54–3.99]	4.57 [5.41–3.80]	4.37 [5.31–3.69]	< 0.001
TG, mmol/L	1.81 [2.74–1.20]	1.53 [2.23–1.14]	1.47 [2.05–1.06]	1.44 [1.96–1.05]	< 0.001
HDL, mmol/L	1.06 [1.24–0.930]	1.12 [1.31–0.960]	1.12 [1.30–0.960]	1.14 [1.34–0.970]	< 0.001
LDL, mmol/L	3.17 [3.73–2.64]	3.01 [3.61–2.43]	2.91 [3.53–2.30]	2.76 [3.45–2.18]	< 0.001
UACR, mg/g	10.5 [29.8–6.13]	11.6 [38.2–6.36]	13.0 [46.7–6.86]	18.7 [68.8–8.66]	< 0.001
eGFR, mL/min per 1.73 m^2	115 [126 – 103]	105 [113 – 94.0]	98.3 [106 – 85.7]	88.6 [97.8–71.7]	< 0.001
DKD, %	316(29.4%)	324(30.3%)	360(33.8%)	470(43.8%)	< 0.001

DKD Diabetic kidney disease, SBP Systolic blood pressure, DBP Diastolic blood pressure, TC Total cholesterol, TG Triglycerides, HDL High-density lipoprotein, LDL Low-density lipoprotein, UACR Urine albumin to creatinine ratio, eGFR Estimated glomerular infiltration rate, ePWV Estimated pulse-wave velocity

model. Multivariable-adjusted logistic regression models were employed to examine the relationship between ePWV and the prevalence of DKD, UACR ≥ 30 mg/g and eGFR < 60 mL/min per 1.73 m^2, with odds ratios (OR) and 95% confidence intervals (CIs) provided. Restricted cubic spline (RCS) analysis was utilized to explore the dose-response relationship between ePWV and the prevalence of DKD, UACR ≥ 30 mg/g and eGFR < 60 mL/min per 1.73 m^2. To explore potential effect moderators, patients were stratified into subgroups based on age (< 60 or ≥ 60 years), sex (male or female), duration of diabetes (< 10 or ≥ 10 years), and presence of hypertension (yes or no).

Results

Table 1 displays the general and sociodemographic characteristics of the participants in the study. The analysis ultimately encompassed 4,296 individuals with diabetes. Out of these, 2,821 (65.6%) were identified as Non-DKD, whereas 1,475 (34.4%) were diagnosed with DKD. Compared to the Non-DKD group, individuals with DKD showed significantly higher levels across multiple parameters, including age, male population, diabetes duration, SBP, HbA1c, total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), UACR, and ePWV. While high-density lipoprotein (HDL) and eGFR were notably lower in the DKD group compared to their Non-DKD counterparts.

Table 2 delineates the characteristics of participants, organized by quartiles of ePWV. Participants within the highest ePWV quartile, relative to those in the lowest

Table 3 The determinants of DKD in patients with T2DM

Clinical characteristics	Univariate		Multivariate	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, years	1.02 (1.01–1.02)	< 0.001	0.99 (0.97–1.01)	0.319
Men, %	1.23 (1.08–1.40)	0.001	1.45 (1.26–1.67)	< 0.001
Duration of diabetes, years	1.03 (1.02–1.03)	< 0.001	1.02 (1.01–1.03)	< 0.001
SBP, mmHg	1.01 (1.01–1.02)	< 0.001	0.99 (0.98–1.00)	0.230
DBP, mmHg	1.00 (0.99–1.01)	0.900		
HbA1c, %	1.08 (1.05–1.12)	< 0.001	1.08 (1.04–1.12)	< 0.001
TC, mmol/L	1.13 (1.08–1.19)	< 0.001	1.11 (0.85–1.45)	0.434
TG, mmol/L	1.18 (1.13–1.22)	< 0.001	1.17 (1.10–1.25)	< 0.001
HDL, mmol/L	0.70 (0.55–0.88)	0.002	0.71 (0.49–1.02)	0.067
LDL, mmol/L	1.13 (1.06–1.22)	< 0.001	1.04 (0.75–1.42)	0.826
ePWV, m/s	1.17 (1.13–1.21)	< 0.001	1.35 (1.14–1.59)	< 0.001

SBP Systolic blood pressure, DBP Diastolic blood pressure, TC Total cholesterol, TG Triglycerides, HDL High-density lipoprotein, LDL Low-density lipoprotein, ePWV Estimated pulse-wave velocity

Table 4 The associations between ePWV levels and the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2

	ePWV, m/s				$P_{for\ trend}$	Total	P_{value}
	Quartile 1	Quartile 2	Quartile 3	Quartile 4			
The prevalence of DKD							
Model 0 OR(95% CIs)	Ref.	1.04 (0.87–1.26)	1.23 (1.02–1.47)	1.87 (1.57–2.24)	< 0.001	1.17(1.13, 1.21)	< 0.001
Model 1 OR(95% CIs)	Ref.	0.92 (0.74–1.15)	1.01 (0.78–1.29)	1.32 (0.96–1.81)	0.025	1.23 (1.15–1.31)	< 0.001
The prevalence of UACR ≥ 30 mg/g							
Model 0 OR(95% CIs)	Ref.	1.16 (0.96–1.41)	1.37 (1.13–1.65)	1.82 (1.51–2.19)	< 0.001	1.15(1.12, 1.19)	< 0.001
Model 2 OR(95% CIs)	Ref.	1.08 (0.86–1.36)	1.19 (0.91–1.55)	1.39 (1.00-1.93)	0.032	1.20 (1.12–1.29)	< 0.001
The prevalence of eGFR < 60 mL/min per 1.73 m^2							
Model 0 OR(95% CIs)	Ref.	0.92 (0.67–1.26)	0.90 (0.65–1.23)	2.09 (1.58–2.75)	< 0.001	1.22(1.16, 1.28)	< 0.001
Model 2 OR(95% CIs)	Ref.	0.67 (0.46–0.96)	0.56 (0.37–0.85)	0.99 (0.60–1.62)	0.509	1.21 (1.08–1.34)	< 0.001

DKD Diabetic kidney disease, UACR Urine albumin to creatinine ratio, eGFR Estimated glomerular infiltration rate, ePWV Estimated pulse-wave velocity

Model 0 The model was not adjusted

Model 1 The model was adjusted for age, sex, duration of diabetes, HbA1c, TC, TG, HDL, and LDL

quartile, were generally older, had a higher prevalence of being female and DKD, and showed increased levels of diabetes duration, SBP, DBP, HDL, and UACR. Moreover, in the highest ePWV quartile compared to the lowest, lower levels of HbA1c, TC, TG, LDL, and eGFR were observed.

The determinants of DKD in patients with T2DM are reported in Table 3. DKD correlated positively with age, the male gender, duration of diabetes, SBP, HbA1c, TC, TG, LDL, and ePWV, but negatively with HDL levels in univariate linear regression analysis. Further multivariate analysis showed that the increased prevalence of DKD was associated with being male, high duration of diabetes, high HbA1c, high TG, and high ePWV.

We devised two models to evaluate the independent impact of ePWV on the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2. As illustrated in Table 4, a higher ePWV was linked to a greater prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2, even when adjusting for a range of confounding factors, including age, sex, duration of diabetes, HbA1c, TC, TG, HDL, and LDL. When comparing individuals in the highest ePWV quartile to those in the first quartile, the prevalence of DKD, and UACR ≥ 30 mg/g was significantly higher by 32%, and 39% respectively after adjusting for these confounding factors. Each unit increase in ePWV was associated with a 23%, 20% and 21% increase in the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2 in T2DM participants, respectively, after adjusting for the same confounding factors.

The distinct clinical phenotypes of DKD were then clearly defined and quantified, as shown in Table 5: patients with UACR ≥ 30 mg/g and eGFR ≥ 60 mL/min/1.73 m^2; patients with UACR ≥ 30 mg/g and eGFR < 60 mL/min/1.73 m^2 (representing "classic" diabetic kidney disease); and patients with UACR < 30 mg/g and eGFR < 60 mL/min/1.73 m^2. The number and percentage of participants in these three phenotypes were 1072 (72.7%), 235 (15.9%), and 168 (11.4%), respectively. We found that ePWV was associated with DKD across all three phenotypes, and this association remained significant even after adjusting for confounding factors.

Table 5 The associations between ePWV levels and different clinical phenotypes of DKD

Different clinical phenotypes of DKD	ePWV, m/s			
	Model 0		Model 1	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
UACR ≥ 30 mg/g, and eGFR ≥ 60 mL/min per 1.73 m^2	1.10 (1.06–1.14)	< 0.001	1.15 (1.07–1.24)	< 0.001
UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2	1.26 (1.18–1.35)	< 0.001	1.19 (1.04–1.37)	0.009
UACR < 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2	1.13 (1.05–1.22)	0.002	1.18 (1.01–1.38)	0.038

DKD Diabetic kidney disease, UACR Urine albumin to creatinine ratio, eGFR Estimated glomerular infiltration rate, ePWV Estimated pulse-wave velocity

Model 0 The model was not adjusted

Model 1 The model was adjusted for age, sex, duration of diabetes, HbA1c, TC, TG, HDL, and LDL

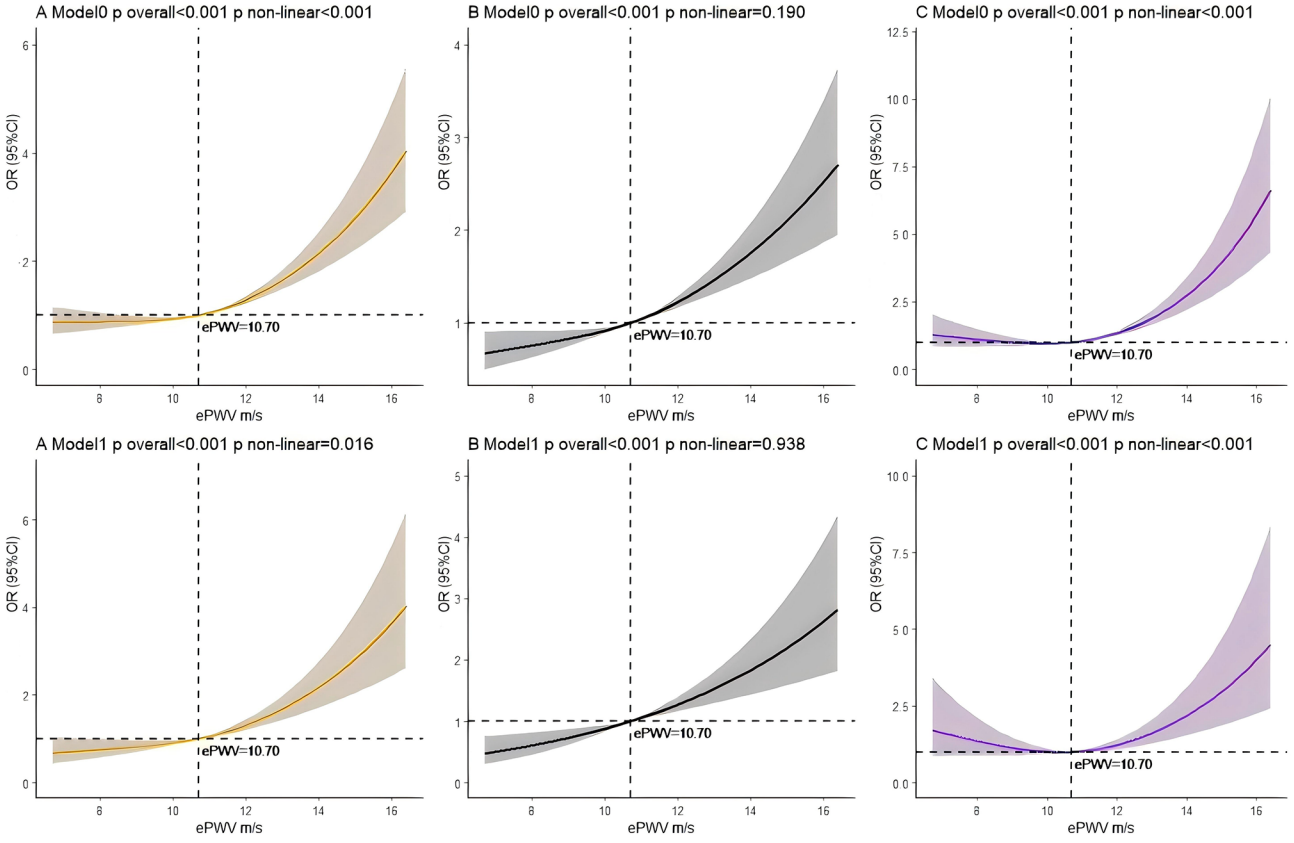

Fig. 1 RCS analysis of ePWV in relation to the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2. **A**: DKD **B**: UACR ≥ 30 mg/g **C**: eGFR < 60 mL/min per 1.73 m^2. Model 0 The model was not adjusted. Model 1 The model was adjusted for age, sex, duration of diabetes, HbA1c, TC, TG, HDL, and LDL

RCS curves were utilized to evaluate the dose-response relationship between ePWV and the prevalence of DKD, UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2. As illustrated in Fig. 1, a J-shaped relationship was observed between ePWV and the prevalence of DKD and eGFR < 60 mL/min per 1.73 m^2, even after adjusting for age, sex, duration of diabetes, HbA1c, TC, TG, HDL, and LDL. Additionally, the analysis revealed a linear association between ePWV and the prevalence of UACR ≥ 30 mg/g, after controlling for the same confounding factors.

As illustrated in Fig. 2, we stratified the analyses by age (< 60 or ≥ 60 years), sex (male or female), duration of diabetes (< 10 or ≥ 10 years), and presence of hypertension (yes or no) to examine whether these potential confounders influenced the associations between ePWV and the prevalence of DKD, and to evaluate any interactions. The results of these stratified analyses demonstrated that the associations between ePWV and the prevalence of DKD were generally consistent across all sub-populations. However, significant interactions were observed between ePWV and age for DKD in participants and statistically significant associations were only observed in participants older than 60 years.

Subgroups	n	OR	95% CIs	*P* value	p for interaction
Age					
<60	1971	1.35	0.978, 1.875	0.068	0.002
≥60	1962	1.67	1.363, 2.043	0.000	
Gender					
male	2196	1.62	1.362, 1.973	0.000	0.079
female	1737	1.82	1.495, 2.214	0.000	
Deration of diabetes					
≤10	1528	1.48	1.171, 1.864	0.001	0.188
>10	2768	1.59	1.364, 1.861	0.000	
Hypertension					
Yes	2046	1.29	1.073, 1.545	0.007	0.109
No	2250	1.88	1.532, 2.298	0.000	

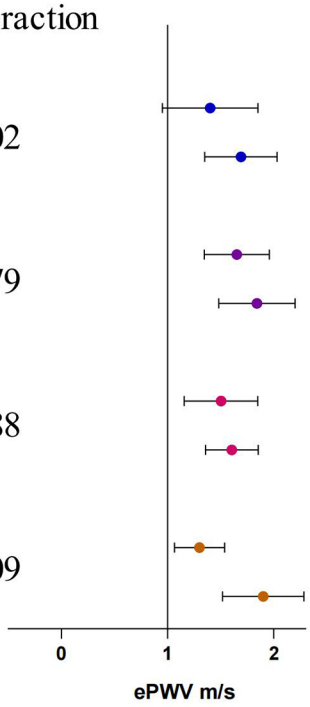

Fig. 2 Subgroup analysis for the associations between ePWV and the prevalence of DKD

Discussion

Based on retrospective data from Guan'anmen hospital between 2017 and 2022, we included 4,296 patients with T2DM and revealed for the first time an independent positive correlation between ePWV and the prevalence of DKD in this population. This association was confirmed after adjusting for multiple confounding factors. Additionally, we observed a significant interaction with age in the relationship between ePWV and DKD prevalence, with the correlation being significant only in individuals aged 60 years or older.

Although CfPWV is regarded as the gold standard for diagnosing arterial stiffness, its measurement is highly complex. Participants must refrain from caffeine intake for at least 3 h before the test and maintain a supine position for 10 min. Additionally, the measurement tools, which often involve sophisticated physical control systems, are relatively expensive and require a high level of technical expertise from the operator [19]. These factors have limited its widespread use in clinical practice. In 2010, the concept of ePWV (estimated pulse wave velocity) was introduced as a new metric for assessing arterial stiffness, calculated using age and mean blood pressure [20]. Research has shown that ePWV closely correlates with cfPWV and exhibits high sensitivity and specificity for detecting aortic stiffness [13, 21]. As a result, ePWV offers a non-invasive, simple method for assessing arterial stiffness, unlike traditional methods requiring specialized equipment. Estimated using routine blood pressure data, ePWV provides a cost-effective alternative suitable for broad clinical screening. Additionally, it introduces arterial stiffness as a novel predictive factor for DKD, broadening traditional risk prediction perspectives that have focused on glucose control and proteinuria. By reflecting both vascular and kidney health, ePWV lowers testing barriers and enables earlier DKD screening. Integrated with large-scale patient datasets, ePWV supports big-data analysis for more individualized DKD assessments across diabetic subgroups, accommodating various disease stages.

The clinical predictive value of ePWV has been confirmed across various diseases. A prospective cohort study involving 5,325 diabetic patients underscored the importance of ePWV, revealing that each 1 m/s increase in ePWV was associated with a 53–102% increase in mortality risk for diabetic individuals, suggesting that ePWV could be an effective tool for assessing mortality risk in diabetic patients [22]. A cross-sectional study from South Korea showed that elevated baPWV is associated with the occurrence of albuminuria and a decline in eGFR in patients without albuminuria. However, after adjusting for several key clinical variables such as BMI, glycated hemoglobin, systolic blood pressure, pulse pressure, and duration of diabetes, baPWV was found to be unrelated to eGFR in T2DM patients with either normal albuminuria or albuminuria [23]. We found that each unit increase in ePWV was associated with a 23%, 21% and 25% increase in the prevalence of DKD,

UACR ≥ 30 mg/g, and eGFR < 60 mL/min per 1.73 m^2 in T2DM participants, respectively, after adjusting for various confounding factors. A J-shaped relationship was observed between ePWV and the prevalence of DKD and eGFR < 60 mL/min per 1.73 m^2, and a linear association between ePWV and the prevalence of UACR ≥ 30 mg/g. Notably, we found that ePWV is associated with all three phenotypes of diabetic DKD. Additionally, our results identified other confounding factors independently associated with DKD, including gender, duration of diabetes, HbA1c, and TG, which are consistent with previous research findings [24].

Based on existing literature and our research findings, we hypothesize that the correlation between ePWV and DKD is influenced by the impact of arterial stiffness on the development of DKD. Chronic hyperglycemia in patients with type 2 diabetes leads to long-term low-grade inflammation. As inflammatory signaling pathways become increasingly activated, oxidative stress and the accumulation of advanced glycation end products (AGEs) rise. These factors drive the continuous proliferation and expansion of vascular endothelial cells, resulting in the production of harmful substances. Concurrently, the enzyme systems within endothelial cells become activated, causing damage to the vascular intima. This leads to reduced vessel wall elasticity and increased vascular stiffness, ultimately causing vascular damage and arterial sclerosis. As arterial sclerosis progresses, it affects the small arteries of the glomeruli in the kidneys, leading to glomerular changes characterized by hypertrophy and hyperfiltration. This impairs the filtering capacity of the glomeruli, which is reflected in a decrease in eGFR. Additionally, damage to the glomerular filtration barrier increases its permeability, allowing large molecules such as albumin to escape, resulting in an elevated UACR [25–27]. This mechanism aligns with our findings. The decline in eGFR and the occurrence of proteinuria together promote the development of DKD [28]. As a chronic condition, arterial sclerosis is well-documented in its association with kidney damage, such as increasing cardiovascular or all-cause mortality risk in dialysis patients, or being linked to early declines in kidney function [29–33].

Additionally, our subgroup analysis revealed that age is a strong confounding factor in the cross-sectional association between ePWV and DKD, with ePWV increasing as age advances. It is well known that aging is an independent risk factor for both hypertension and arterial stiffness. In younger individuals, there is a stiffness gradient between the aorta and muscular arteries, but with aging, this gradient diminishes as elastic fibers degenerate and are replaced by collagen fibers in the vessel walls. This process leads to vascular remodeling and dysfunction [34]. Age-related arterial stiffness is a major contributor to declining kidney function. A Japanese cohort study [35] found that advanced age, lower diastolic blood pressure, and higher baPWV are potential risk factors for DKD. Another cohort study conducted among an elderly general population in China [36] showed that both cfPWV and baPWV are significantly associated with age. After adjusting for confounding factors, the study found that both cfPWV and baPWV were significantly positively correlated with urinary microalbumin. Our study observes an association between ePWV and DKD, but this finding only suggests that arterial stiffness may play a role in the pathogenesis of chronic kidney damage, especially in older patients with type 2 diabetes. This hypothesis requires further research for verification.

Our study, a large-scale investigation involving inpatients, ensures a substantial sample size while rigorously controlling participant information. We have made efforts to adjust for confounding factors to produce more reliable results. However, our study has limitations. First, the absence of body mass index (BMI) data may limit a comprehensive understanding of the ePWV-DKD relationship. Second, due to limitations in medical resources, we were unable to provide detailed information in the manuscript comparing CfPWV by Doppler ultrasound and baPWV with ePWV. Third, as a cross-sectional study, it cannot infer causality. We agree that longitudinal studies are necessary to further explore ePWV's predictive capability, especially through dynamic monitoring of ePWV changes over time in diabetic patients without DKD. This would allow us to evaluate its early warning value before DKD onset. Such a design would also help establish appropriate ePWV risk thresholds, enabling more precise identification of potential high-risk individuals.

Conclusion

After adjusting for potential confounding factors, our analysis identified a significant association between higher ePWV levels and the increased prevalence of DKD, UACR ≥ 30 mg/g and eGFR < 60 mL/min per 1.73 m^2. These insights underscore the potential benefits of monitoring ePWV levels—a simple, cost-effective, and broadly accessible approach—for the early detection of DKD.

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Author contributions

Shuwu Wei and Xinyu Pan conceived the study, participated in its design and coordination, analyzed the data and drafted the manuscript. Yao Xiao recruited patients and collected data. Junping Wei participated in its design and coordination, and was responsible for project administration and visualization. All authors read and approved the final version of manuscript.

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Data availability
The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate
This retrospective study was approved by the Medical Ethics Committee of Guang'anmen Hospital, which is affiliated with the China Academy of Chinese Medical Sciences (Approval No. 2023-187-KY). The ethics committee has waived the requirement of informed consent for this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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