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RESEARCH

Association of weight-adjusted waist index and diabetic kidney disease in type 2 diabetes mellitus

Yunyi Ding[1,*], Siyao Lv[2,*], Ruijie Xie[3], Wei Ye[4], Yichen Luo[5] and Yayu Li[6]

[1]Department of Nephrology, Hangzhou TCM Hospital of Zhejiang Chinese Medical University, Hangzhou, China
[2]Department of Gastroenterology, Hangzhou TCM Hospital of Zhejiang Chinese Medical University, Hangzhou, China
[3]Division of Clinical Epidemiology and Aging Research, University of Heidelberg, Heidelberg, Germany
[4]Department of Gastroenterology, Hangzhou TCM Hospital, Hangzhou, China
[5]School of Mechanical Engineering, Zhejiang University, Hangzhou, China
[6]Department of Nephrology, Hangzhou TCM Hospital, Hangzhou, China

Correspondence should be addressed to W Ye or Y Luo or Y Li: yewei7752@163.com or luoyichen@zju.edu.cn or liyayu@zcmu.edu.cn

*(Y Ding and S Lv contributed equally to this work)

Abstract

Objective: The aim of this study was to investigate the relationship between weight-adjusted-waist index (WWI) and diabetic kidney disease in individuals afflicted with type 2 diabetes.

Methods: Comprehensive data were ascertained from the National Health and Nutrition Examination Survey in 2013–March 2020. Weighted univariate, multivariate logistic regression models, subgroup analyses and tests for interaction were performed. Additionally, we employed smooth curve fitting to assess linear correlations and the threshold effects were calculated by applying a binary linear regression model. Breakpoints are identified by a model with maximum likelihood ratio and a two-step recursive approach. Receiver operating characteristic curve (ROC) along with the area under the curve (AUC) value predict the capability of WWI and body mass index for diabetic kidney disease.

Results: A total of 10,661 individuals diagnosed with type 2 diabetes were included, and the overall prevalence of diabetic kidney disease was 20.74%. WWI exhibited a positive correlation with the likelihood of diabetic kidney disease in type 2 diabetes patients (OR: 1.17, 95% CI: 1.03–1.33). The results of subgroup analysis showed significant interaction for gender ($P < 0.05$). Among female patients, U-shaped correlations were observed with a breakpoint at 11.48. Additionally, weight-adjusted waist index (AUC = 0.664) proved to be a more effective predictor of diabetic kidney disease compared to body mass index (AUC = 0.555).

Conclusion: In patients with type 2 diabetes, increased weight-adjusted-waist index is implicated with an increased risk of diabetic kidney disease. WWI can be used as a new anthropometric index to predict diabetic kidney disease, and its predictive ability is stronger than body mass index.

Keywords: weight-adjusted waist index; obesity; diabetic kidney disease; NHANES; cross-sectional study

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Introduction

Over the preceding three decades, there has been a fourfold global escalation in the prevalence of diabetes mellitus, culminating in approximately 1 out of 11 adults being diagnosed with this condition, a substantial 90% of whom are affected by type 2 diabetes (T2D) (1). T2D is a chronic ailment characterized by its potential to instigate both macrovascular and microvascular damage (2), thereby facilitating the onset of an array of complications encompassing diabetic kidney disease (DKD), diabetic retinopathy, and cardiovascular and cerebrovascular disease. These complications are intimately associated with an augmentation in disability rates, a diminution in the quality of life, and a contraction in life expectancy (3, 4). It is noteworthy that approximately 20% of individuals diagnosed with diabetes mellitus may experience a progression to DKD (5), a condition which has emerged as the primary etiological factor underlying end-stage renal disease (ESRD) in the USA (6). Obesity is closely related to DKD. In 1974, Weisinger *et al.* first reported that severe obesity could lead to massive proteinuria (7). Since then, several animal experimental models and clinical studies have confirmed that obesity can cause kidney damage independent of diabetes, that is, obesity-related glomerulopathy. Current epidemiological studies have found that obesity and overweight are significantly related to microalbuminuria (8, 9, 10), but the mechanism still needs to be further studied. Clearly, obesity management in patients with DKD is particularly important.

Obesity is a complex multifactorial disease. The global prevalence of overweight and obesity has undergone a tripling augmentation since 1980, culminating in about a third of the global populace being classified under these categories (11, 12). Literature pertaining to obesity extrapolates that nearly half of the adult demographic in the USA is poised to be categorized as obese by 2030 (13). It is imperative to note that obesity is inextricably linked to a multitude of pathologies, encompassing, but not restricted to hypertension, diabetes mellitus, cardiovascular ailments, and oncological conditions (12, 14, 15). Both overweight and obesity have been identified as contributory factors in the initiation and progression of T2D and its attendant complications (16, 17, 18). Presently, obesity is perceived as a multifaceted and heterogeneous chronic disorder, with manifestations that do not exhibit uniformity across patients, necessitating personalized therapeutic approaches and sustained support akin to other complex chronic conditions (16). Therefore, there is an urgent requirement for a validated and accurate parameter to assess obesity.

Currently, commonly used body fat indices for clinical assessment of obesity include waist circumference (WC), waist-to-hip ratio (WHR) body mass index (BMI), and waist-to-height ratio (WHtR) (18, 19, 20). Studies have found that adipose tissue distribution, rather than actual body fat, may play a more important role in all-cause mortality (20, 21). While BMI is prevalently employed as a tool for the evaluation and classification of obesity, it harbors a significant limitation in its incapacity to discern between adipose tissue and lean mass, as well as between central and peripheral fat deposition. WC serves as an indicator of abdominal obesity, albeit its failure to differentiate between subcutaneous and visceral fat, is largely attributable to height variation. WHR and WHtR provide a more precise depiction of abdominal obesity, nevertheless, these metrics have limitations in differentiating between subcutaneous and visceral fat (22). We notice that weight-adjusted waist index (WWI), introduced by Park *et al.* (23), is an innovative obesity index computed as WC divided by the square root of body weight (WC/weight$^{1/2}$). It appears that WWI amalgamates the benefits of WC, while concurrently attenuating its relevance with BMI, thereby serving primarily as an indicator of central obesity (24). Existing literature has indicated that WWI embodies potent predictive capabilities pertaining to cardiometabolic morbidity and mortality (18, 20, 23). Additionally, an investigation conducted in a Korean cohort revealed a direct relationship between WWI and fat mass, juxtaposed against an inverse association with muscle mass (25).

Obesity is demonstrably linked with DKD, and a great deal of research has elucidated the association between BMI and the incidence of DKD (26, 27, 28). Conversely, the relationship between WWI and the occurrence of DKD has not undergone a comprehensive investigation. In light of this knowledge gap, we undertook an analysis of the association between WWI and DKD, though obtained and utilized the data in the database from the National Health and Nutrition Examination Survey (NHANES) spanning the period from 2013 to March 2020. The findings emanating from our investigation hold the potential to furnish substantiation that can be instrumental in fortifying strategies geared towards the early identification, prophylaxis, and management of complications associated with diabetes.

Methods

Study population

NHANES is a nationally representative survey aimed at gathering information about underlying health risk factors and the nutrient status of nonhospitalized populations in the USA. The data analyzed in this study were collected in the NHANES (2013–March 2020). This is a cross-sectional study employing a stratified, multi-stage probability cluster sampling methodology to ensure that our research sample is sufficiently representative (29). Data collected on NHANES were approved by the National Center for Health Statistics Research Ethics Review Committee, with all subjects providing their knowledgeable written consent.

Our analysis initially included 35,706 participants. However, based on exclusion criteria, we excluded people under 20 years of age (n = 14,986), no weight or WC data were available to calculate WWI (total, n = 2297; Body weight, n = 18; WC, n = 2279), missing urinary albumin/creatinine ratio (ACR) information (n = 223) and estimated glomerular filtration rate (eGFR) information (n = 931), T2DM (n = 6501), and pregnant individuals (n = 107). Subsequently, 10,661 eligible adult participants were included in our final analysis (Fig. 1).

Research data and variables

The WWI is a composite index based on WC and body weight and can be used for central obesity assessment. We obtained accurate measurements of patients' WC and weight from the NHANES database by professionally tested health professionals. Subsequently, WWI was calculated using the formula: divide WC by the square root of body weight, with the calculated figures retained at two decimal places (WWI = WC/body weight$^{1/2}$, where WC was in centimeters while weight was in kilograms). The degree of central obesity is represented by WWI; the higher the value of WWI, the more significant the degree of obesity. And we use WWI as the exposure variable in this analysis.

Diabetes was delineated as per the following criteria: a precedent diagnosis by a health-care professional, fasting glucose in plasma levels are equivalent to or greater than 126 mg/dL, random blood glycemic levels equal to or above 200 mg/dL, glycosylated hemoglobin levels equal to or surpassing 6.5%, or the administration of pharmacological agents for diabetes management. The eGFR was ascertained by employing the Chronic Kidney Disease Epidemiology Collaboration algorithm (30). DKD is defined as diabetes with the presence of albuminuria, impaired GFR, or both. The diagnostic criteria for DKD in T2D patients encompassed an ACR equal to or greater than 30 mg/g and/or an eGFR below 60 mL/min/1.73 m² (31, 32). In our survey, DKD served as an outcome variable.

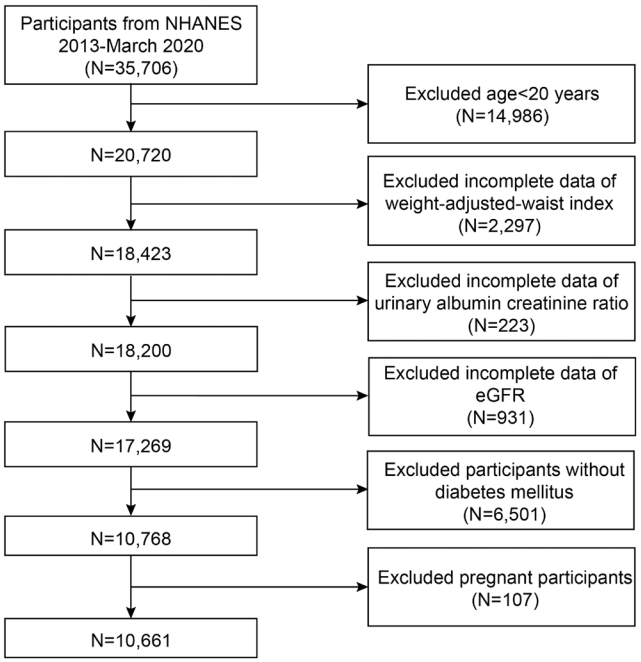

Figure 1

Participant selection flowchart. NHANES, National Health and Nutrition Examination Survey. eGFR, estimated glomerular filtration rate.

In addition, we considered a range of covariates, including patient age, gender, education, race, insulin use, and glucose-lowering medication use. Anthropometric and laboratory variables were also taken into account, including fasting blood glucose (mg/dL) and glycated hemoglobin (%), which are the most commonly measured in diabetic patients, as well as a number of blood tests, such as white blood cell count (1000 cells/μL), platelet count (1000 cells/μL), and hemoglobin (g/dL), and markers that are closely related to the kidneys function, such as ACR (mg/g), serum creatinine (mg/dL), serum uric acid (mg/dL), eGFR (mL/min/1.73 m^2), and others related to obesity, metabolism, such as total cholesterol (mg/dL), triglycerides (mg/dL), high-density lipoprotein (HDL) cholesterol (mg/dL), low-density lipoprotein (LDL) cholesterol (mg/dL), and BMI. The diagnosis of hypertension was made on the basis of any of the following standards: currently applying prescribing of antihypertensive medications, diagnosed hypertension, or three consecutive measurements of upper blood pressure (systolic) at or over 140 mm Hg or lower blood pressure (diastolic) at or exceeding 90 mm Hg (33). It is necessary to emphasize that measurements of lipid profiles were collected only in participants who had been fasting for not fewer than 8.5 h but not exceeding 24 h, thus guaranteeing the precision of these evaluations. More detailed figures are open to public inspection at https://www.cdc.gov/nchs/nhanes/ (accessed October 17, 2023).

Methods of statistical analysis

To discern differences in baseline characteristics between non-DKD and DKD cohorts among T2D patients, the weighted Student's t-test was applied to continuous variables, whereas the weighted chi-square test was employed for categorical variables. Multivariate logistic regression analysis was used to assess the link between WWI and DKD. For potential nonlinear correlations between WWI and DKD, weighted generalized additive models and smoothed curve fitting were deployed. When the above analyses identified nonlinear associations, a two-stage linear regression model, also referred to as a segmental regression model, was used to fit each segment together with an assessment of threshold effects. A log-likelihood ratio test was performed on a unilineal (nonsegmented) model and a two-stage

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linear regression model to ascertain the presence of a threshold. The breakpoint (K), which serves to unify the components, depends on the model that provides the maximum likelihood ratio and was ascertained through a two-step recursive approach. To clarify the relationship between WWI and DKD across different demographic subsets, we used two analytical approaches, including stratified analyses and interactive tests. Analogously, the judgment of WWI and BMI for DKD was assessed by calculating the area under the curve (AUC) employing the Receiver Operating Characteristic curve (ROC). The threshold of significance for statistics was a bilateral *P*-value of less than 0.05. All statistical analyses applied in this study were performed in R software (version 4.2) and in conjunction with EmpowerStats (version 4.1).

Results

Characteristics of the baseline

A total of 10,661 participants were included in our research, their mean age was 48.86 ± 17.00 years. The gender distribution was in a generally homogeneous manner, of which 49.47% were males and 50.53% were females. The overall prevalence of DKD in T2D was 20.74% (weighted proportion).

The findings suggest that CKD patients among participants were more likely to be female, non-Hispanic white, less educated, hypertensive, and use insulin or glucose-lowering medications. Additionally, it was observed that the rate of DKD developed with age, dysglycemia (including fasting glucose, glycated hemoglobin), markers closely related to renal function (ACR, serum creatinine, and serum uric acid), metabolic disorders targets (triglycerides, BMI), white blood cell count, and WWI levels increased, and meanwhile the hemoglobin, platelet count, eGFR, HDL cholesterol, and LDL cholesterol decreased ($P < 0.05$) (Table 1).

The association between WWI and DKD

The results of the multivariate logistic regression analysis using the three models are presented in Table 2. As shown in the table, WWI was significantly and positively associated with the probability of developing DKD ($P < 0.05$). After full adjustment, for every unit increase in WWI, the risk of patients developing DKD increased by 17% (OR: 1.17, 95% CI: 1.03–1.33). We categorized WWI into three tertiles by value, and people belonging to the highest tertile of WWI had a significantly higher risk of DKD, 36% higher than patients in the lowest tertile (OR: 1.36, 95% CI: 1.07–1.74) (Table 2). In addition, a generalized model using smoothed curve fitting confirm the nonlinear relationship between WWI and DKD. Ultimately, we concluded our findings that there is a nonlinear positive correlation between WWI and DKD (Fig. 2).

Subgroup analyses

To verify the homogeneity of the association between WWI and DKD in the general population and to ascertain crowd-specific, subgroup analyses and interaction tests according to age, gender, hypertension, insulin use, and glucose-lowering medication use were also performed in our study (Table 3).

However, this association is not consistent in terms of findings. We detected significant interaction for gender ($P < 0.05$), while there was no statistical significance for age, hypertension, insulin use, and glucose-lowering drug use (all P for interaction >0.05). WWI and DKD remained positively associated in male, 20–44 and 45–59 age subgroups, non-hypertension subjects. In summation, the result of our findings signifies that the association between WWI and DKD exhibits gender dependence ($P < 0.05$) and that the positive association was only present among males but not among females (P for interaction <0.05).

Nonlinear association of WWI and DKD in females

Our analysis was further augmented by employing generalized additive models and smooth curve fittings to assess potential non-linearity across different strata. There was no evidence of nonlinearity in the relationship between WWI and DKD when stratified by variables such as age, hypertension status, insulin use, and glucose-lowering drug use. However, when stratified by gender, the resulting curve denoted the presence of a nonlinear relationship amongst the female cohort (Fig. 3). Through the application of a two-piecewise linear regression model, the breakpoint (K) was ascertained to be 11.48 for females. To the right of this breakpoint, there existed a positive correlation between WWI and DKD (OR = 1.45, 95% CI: 1.09–1.92), whereas to the left, an inverse correlation was observed (OR = 0.60, 95% CI: 0.42–0.86) (Table 4).

The discrimination powers of WWI and BMI on DKD

ROC curve analysis showed that the AUCs of WWI and BMI on DKD were 0.664 and 0.555, respectively ($P < 0.001$). When the cutoff WWI value was set as 11.37, a sensitivity of 61.55% and a specificity of 62.18% on DKD, respectively. When the cutoff BMI value was set as 31.30, a sensitivity of 43.67% and a specificity of 64.91% on DKD, respectively (Fig. 4).

Discussion

The objective of this study was to evaluate the association between WWI and DKD in T2DM in the USA. 10,661 patients diagnosed with T2D were included in our

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Table 1 Basic characteristics of participants with T2D.

	Non-DKD	DKD	
Characteristics	***n* = 8450**	***n* = 2211**	***P* for trend**
Age (years)	46.38 ± 16.14	60.71 ± 16.00	<0.001
Sex, *n* (%)			0.001
Male	49.96	45.75	
Female	50.04	54.25	
Race/ethnicity, *n* (%)			<0.001
Mexican American	9.51	7.31	
Other Hispanic	7.03	5.15	
Non-Hispanic White	63.45	66.82	
Non-Hispanic Black	11.06	12.14	
Other races	8.94	8.58	
Education level, *n* (%)			<0.001
Less than high school	12.51	17.00	
High school or GED	22.87	26.80	
Above high school	64.62	56.20	
Hypertension, *n* (%)			<0.001
No	90.56	74.02	
Yes	9.44	25.98	
Insulin use, *n* (%)			<0.001
No	97.13	87.22	
Yes	2.87	12.78	
Glucose-lowering drug use, *n* (%)			<0.001
No	89.10	70.80	
Yes	10.90	29.20	
Fast glucose (mg/dL)	143.18 ± 49.60	163.75 ± 68.68	<0.001
Glycated hemoglobin (%)	5.68 ± 0.95	6.52 ± 1.71	<0.001
White blood cell (1000 cells/μL)	7.68 ± 2.21	8.02 ± 7.11	<0.001
Hemoglobin (g/dL)	14.18 ± 1.41	13.78 ± 1.66	<0.001
Platelets (1000 cells/μL)	243.10 ± 60.12	234.84 ± 67.92	<0.001
Urinary albumin–creatinine ratio (mg/g)	8.25 ± 5.58	228.49 ± 869.53	<0.001
Serum creatinine (mg/dL)	0.85 ± 0.18	1.12 ± 0.74	<0.001
Serum uric acid (mg/dL)	5.29 ± 1.35	5.90 ± 1.63	<0.001
eGFR (mL/min/1.73 m^2)	93.13 ± 15.73	69.97 ± 24.73	<0.001
Total cholesterol (mg/dL)	189.37 ± 41.55	188.46 ± 46.18	0.400
Triglyceride (mg/dL)	140.24 ± 164.50	158.27 ± 141.71	0.020
High-density lipoprotein cholesterol (mg/dL)	52.98 ± 16.36	51.67 ± 18.26	0.002
Low-density lipoprotein cholesterol (mg/dL)	105.07 ± 38.11	100.62 ± 37.61	0.019
BMI (kg/m^2)	29.58 ± 6.94	31.05 ± 7.41	<0.001
WWI	11.01 ± 0.82	11.53 ± 0.79	<0.001

ACR, Urinary albumin–creatinine ratio. BMI, body mass index; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; GED, general educational development; T2D, type 2 diabetes; WWI, weight-adjusted waist index.

cross-sectional study, we concluded that elevated WWI is significantly associated with an increased likelihood of developing DKD. Subgroup analysis and interaction tests showed significant interaction for gender. In females, the association between WWI and DKD was nonlinear and positively correlated which has a breakpoint (WWI = 11.48). WWI was positively associated with the likelihood of DKD on the right side of the breakpoint and negatively associated on the left. This finding suggests that at WWI = 11.48, the incidence of DKD in female patients with T2D may be the lowest.

The escalating prevalence of obesity and diabetes has culminated in DKD emerging as the principal etiological factor for chronic kidney disease (CKD) and ESRD on a global scale (34). Specifically, obesity, with an emphasis on central adiposity, has been implicated as a risk factor for complications associated with diabetes (35). A number of studies have shown that an increase in BMI correlates with an increase in the prevalence of DKD (26, 27, 28). A study of a risk prediction model for DKD based on 20 cohorts demonstrated that with an increment of 5 kg/m^2 in BMI, there was an associated 16% escalation

Table 2 Association between WWI and DKD in patients with T2D.

Exposure	Model 1 (OR (95% CI))	Model 2 (OR (95% CI))	Model 3 (OR (95% CI))
Continuous WWI	2.02 (1.90, 2.14)	1.45 (1.35, 1.56)	1.17 (1.03, 1.33)
WWI classification			
Tertile 1	Reference	Reference	Reference
Tertile 2	2.19 (1.91, 2.51)	1.36 (1.18, 1.58)	1.07 (0.85, 1.35)
Tertile 3	4.04 (3.55, 4.60)	1.94 (1.68, 2.26)	1.36 (1.07, 1.74)

Model 1: Not adjusted for covariates; Model 2: Adjusted for age, sex, and race; Model 3: Adjusted for age, sex, race, education, hypertension, white blood cells, hemoglobin, platelets, serum uric acid, total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol.
DKD, diabetic kidney disease; T2D, type 2 diabetes; WWI, weight-adjusted waist index.

in the risk for developing DKD (36). Although BMI is a commonly used anthropometric parameter, it has the disadvantage of lacking the ability to distinguish between lean and adipose tissue mass. Emerging metrics have been employed to investigate the associations between obesity and DKD. The hypertriglyceridemic waist (HTGW) phenotype is delineated as a state in which increased WC and elevated triglyceride concentrations simultaneously. Results from a cross-sectional study in Shanghai involving 4254 diabetic patients suggested a positive association between HTGW phenotype and CKD among Chinese patients diagnosed with T2D (37). Concurrently, the Chinese Visceral Adiposity Index (CVAI), a nascent devised marker of obesity in the

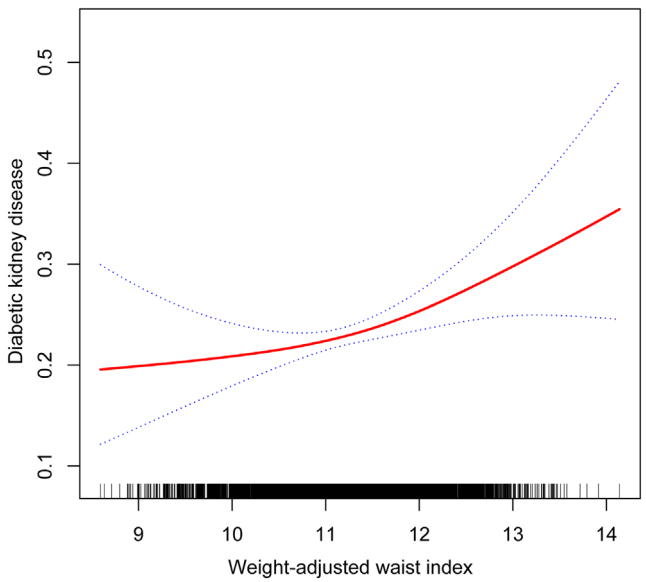

Figure 2

The association between WWI and DKD. The smoothed curve fit between the variables is shown as a solid red line, with the 95% CIs of the fitted results indicated by the blue line. Controlled attenuation parameter.
WWI, weight-adjusted waist index; DKD, diabetic kidney disease.

Table 3 Subgroup analysis of the relationship between WWI and DKD in patients with T2D.

Subgroup	OR (95% CI)	*P* for interaction
Sex		0.033
Male	1.33 (1.12, 1.58)	
Female	1.02 (0.85, 1.22)	
Age (years)		0.143
20–44	1.35 (1.04, 1.75)	
45–59	1.52 (1.19, 1.93)	
≥60	1.16 (0.99, 1.36)	
Hypertension		0.393
No	1.20 (1.04, 1.39)	
Yes	1.06 (0.83, 1.36)	
Insulin use		0.844
No	1.10 (0.96, 1.26)	
Yes	1.15 (0.72, 1.84)	
Glucose-lowering drug use		0.366
No	1.08 (0.93, 1.25)	
Yes	1.23 (0.96, 1.58)	

Age, gender, race, education level, hypertension, white blood cell, hemoglobin, platelets, serum uric acid, triglyceride, HDL cholesterol, total cholesterol, and LDL cholesterol were adjusted. In the subgroup analyses, the models were not tuned for the stratification variables themselves.

abdomen predicated on age, BMI, WC, and metabolic parameters, is deemed to be a superior prognostic indicator for T2D. A Chinese study of 4658 diabetic patients showed that elevated levels of CVAI level were significantly associated with DKD. However, compared with BMI, WC, and other indicators, the calculation of HTGW and CAVI is more complicated. Despite evidence suggesting that these anthropometric measures are correlated with DKD, their validity will need to be confirmed in the future through larger clinical studies and practical applications. Interestingly, a recent population-based study involving 36,921 participants determined that WWI was more closely associated with proteinuria than other measures of obesity, including BMI and WC (24). Considering its straightforward computation and robust efficacy in forecasting disease susceptibility, as a potential anthropometric indicator, the future application of WWI is very promising.

As living standards improve globally, there has been a noticeable rise in the rates of obesity and T2D, which increases the financial burden and affects the quality of life and has gradually become a global public problem. T2D can have a variety of complications such as DKD, diabetic retinopathy, and diabetic foot, among which DKD is an important complication of diabetic microangiopathy (38). The early pathological manifestations of DKD are mainly glomerular hypertrophy, mesangial expansion, and basement membrane thickening, which gradually develop into glomerular and tubulointerstitial fibrosis, and eventually lead to renal failure (39, 40). Obesity is closely related to DKD. Clinical trials have confirmed that moderate weight loss can reduce urinary albumin excretion by about 30% in patients with T2D and

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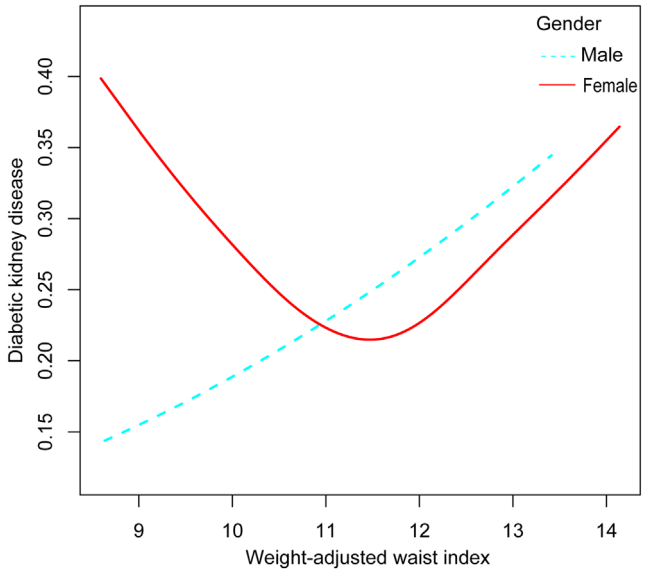

Figure 3

Using a generalized additive model, we determined a nonlinear association between WWI and DKD in the female population. Simultaneously, nonlinear correlations were identified in the female population with a breakpoint of 11.48. On the right side of the breakpoint, the possibility of WWI and DKD was positively correlated, whereas on the left side of the breakpoint, it was negatively correlated. WWI, weight-adjusted-waist index; DKD, diabetic kidney disease.

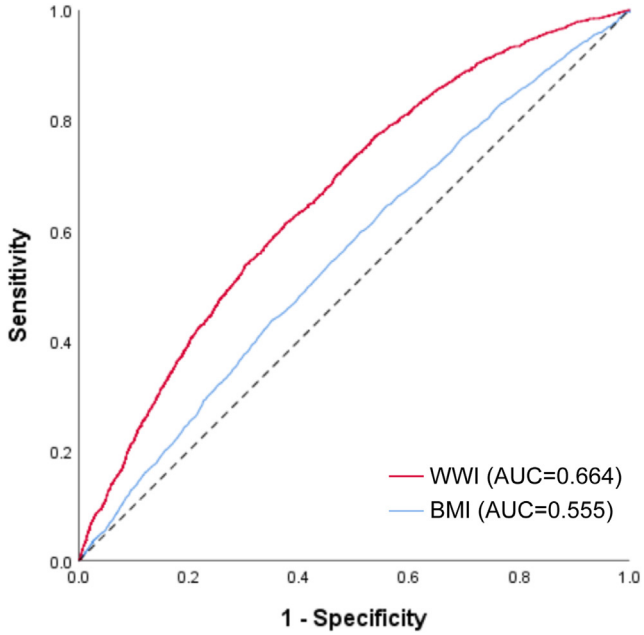

Figure 4

The receiver operating characteristics (ROC) analysis of WWI and BMI on DKD. AUC, the area under the curve. WWI, weight-adjusted-waist index. BMI, body mass index. DKD, diabetic kidney disease.

albuminuria (41). Although the relationship between obesity and DKD remains to be further studied, it is known that many mechanisms are involved in the occurrence and development of obesity affecting DKD. In terms of cellular and molecular mechanisms, adipokines secreted by adipocytes play an important role in the pathogenesis of DKD. A variety of adipokines secreted by adipocytes, such as adiponectin, leptin, resistin, visfatin, and chemerin, are related to the progression of DKD. Adiponectin is considered to have a renoprotective effect, but the serum adiponectin level decreases during the development of some diseases, such as obesity, T2D, metabolic syndrome, and coronary artery disease. Therefore, the renoprotective function of obese patients with T2D is significantly lower than that of nonobese patients, and DKD is more likely to occur. Another example of an inflammatory factor is tumor necrosis factor (TNF), which is a multifunctional proinflammatory cytokine and plays a role in lipid metabolism, lipid accumulation, insulin resistance, and endothelial cell biology and is closely related to the inflammatory response and insulin resistance of DKD (42). Adipocytes can also secrete TNF, which is closely related to the inflammatory response and insulin resistance of diabetes, and further aggravates the development of DKD (43, 44). In addition, obesity itself can cause renal damage. Increasing evidence confirms that obesity-related glomerulopathy can also cause kidney damage in the presence of traditional kidney damage factors of obesity, such as hypertension and T2D (45). In individuals with obesity, the kidneys frequently exhibit deposition of lipids in glomerular and mesangial regions, commonly referred to as foam cells. Accrual of lipids in the glomerular structures triggers an escalation in the expression levels of sterol regulatory element-binding proteins, sequentially, fosters a series of cellular events encompassing the promotion of podocyte apoptosis, proliferation of mesangial cells, and synthesis of cytokines (46).

Table 4 Threshold effects of WWI on DKD were analyzed using two-piece linear regression models.

	Male	Female
Fitting by the standard linear model		
OR (95% CI)	1.33 (1.12, 1.58)	1.02 (0.85, 1.22)
Fitting by the two-piecewise linear model		
Breakpoint (K)	9.74	11.48
OR1 (95% CI)	0.33 (0.06, 1.80)	0.60 (0.42, 0.86)
OR2 (95% CI)	1.37 (1.14, 1.64)	1.45 (1.09, 1.92)
OR2/OR1	4.12 (0.73, 23.31)	2.41 (1.41, 4.11)
Logarithmic likelihood ratio test *P*	0.144	0.001

Age, race, education level, hypertension, white blood cell, hemoglobin, platelets, serum uric acid, total cholesterol, triglyceride, HDL cholesterol, and LDL cholesterol were adjusted.
DKD, diabetic kidney disease; WWI, weight-adjusted waist index.

Our results indicated that female patients with T2D had the lowest incidence of DKD when WWI = 11.48. A recent investigation demonstrated that in females, a phenotype

characterized by elevated total fat mass concomitant with high muscle mass conferred significant protection against cardiovascular mortality (47). This finding contrasts with the prevailing focus on weight reduction as a preventive measure against cardiovascular disease. This led us to envisage whether a certain degree of fat accumulation, in female diabetic patients, has a certain renoprotective effect. In individuals of identical age and body weight, males predominantly accumulate fat through adipocyte hypertrophy, while in females, adipocyte hyperplasia is the prevailing process governing adipocyte pool expansion. Importantly, adipocyte expansion via adipogenesis can mitigate the adverse metabolic consequences of obesity. The hyperplasia of adipose tissue can sustain appropriate vascularization and modulate the levels of insulin-sensitizing, anti-inflammatory hormone adiponectin, along with other metabolically regulated adipokines, which may contribute to ameliorating the renal prognosis in T2D (48). Consequently, a state of healthy obesity characterized by normative adipose immunological and secretory functions may be conducive to the preservation of renal function (49), However, the specific mechanism needs further experimental and clinical research.

Our study has distinct advantages. The large sample drawn from the NHANES dataset, along with our meticulous sample design and weighting factors, results in a representational sample of the U.S. population. This enhances the generalizability of our findings to a larger U.S. population. We employed sophisticated analytical methods, including multivariate logistic regression models, with adjustments for a range of relevant covariates, and investigated the effect of WWI on DKD to minimize bias. Moreover, we delved deeper into the nonlinearity among female participants, thereby illuminating gender differences often overlooked in routine clinical practice. Nevertheless, our study does have inherent limitations. The cross-sectional design restricts our ability to infer causality between WWI and DKD. The cross-sectional design restricts our ability to infer causality between WWI and DKD. Furthermore, despite rigorous adjustment for potential covariates, we must acknowledge that other renal diseases that may cause proteinuria and renal impairment, such as connective tissue disease and hepatitis B-associated nephritis, could not be fully included in our statistics due to the limitations of the NHANES database. Meanwhile, the onset and progression of DKD may result from a combination of factors, including but not limited to the duration of DKD, the use of various glucose-lowering medications, and a wide range of socio-environmental variables. We cannot entirely rule out the impact of these potentially confounding factors. Additionally, missing information in the NHANES dataset, such as participants' general health status and comorbidities, may have a certain impact on our findings. Currently, WWI is less commonly used in clinical applications to assess obesity compared to BMI and WC. Therefore, further research is needed to compare and clarify the strengths and weaknesses of WWI. Finally, due to the nativity of the NHANES database, our findings are essentially restricted to the U.S. population. Thus, the relevance of our findings to different populations or nations outside of the USA needs to be explored in further detail.

Conclusion

Raising WWI may be related to an elevated risk of DKD in T2DM. WWI is positively associated with DKD in males with T2D, but females have a U-shaped association with a breakpoint (WWI = 11.48). Compared with BMI, WWI has a stronger predictive power for DKD, suggesting that obesity assessment through WWI may be beneficial to the early detection of DKD in T2D and that it may be healthier for women to keep their WWI at 11.48. However, further research is required to confirm our findings.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the study reported.

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Author contribution statement
YYD contributed to conception, design, data collection, data analysis, data interpretation and critically revised the manuscript. SYL contributed to conception, design and drafted the manuscript. RJX contributed to conception and critically revised the manuscript. YCL, YYL, and YW contributed to conception and critically revised the manuscript. All authors contributed to the article and approved the submitted version.

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