Original article

Visceral adiposity index is associated with increased urinary albumin excretion: A population-based study

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SUMMARY

Background: The effects of visceral fat accumulation on the renal damage have drawn much attention. We aimed to investigate the possible relationship between visceral adiposity and albuminuria.
Methods: We included information from a population-based study in 9473 subjects aged 40 years or older. As a novel and valid indicator for visceral adipose function, visceral adiposity index (VAI) was determined by gender-specific equations and calculated using simple anthropometric and functional parameters. Increased urinary albumin excretion was defined as albumin-to-creatinine ratio (ACR) 30 mg/g or greater.
Results: The prevalence rate of increased urinary albumin excretion was 6.6% in this population and gradually increased across VAI quartiles. Participants with higher VAI had elevated age, blood pressure, cholesterol, fasting insulin and decreased high density lipoprotein cholesterol and estimated glomerular filtration rate (eGFR) level. In multivariate logistic regression analysis, the adjusted odds ratios (ORs) of increased urinary albumin excretion for increasing VAI quartiles were 1.00 (reference), 1.29 (95% confidence intervals [CI] 0.94—1.76), 1.46 (95% CI 1.08—1.97) and 1.79 (95% CI 1.33—2.41). In subgroup analysis and after multiple adjustments, significant relation between VAI level and prevalent increased urinary albumin excretion was detected in women, younger subjects, non-obesity subjects, those without diabetes and those with eGFR $\geq$60 ml/min per 1.73 m^2.
Conclusion: Visceral fat accumulation evaluating by VAI is independently associated with increased urinary albumin excretion in middle-aged and elderly Chinese.

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1. Introduction

Albuminuria has emerged as a major public health concern because of its significant impact on future unfavorable clinical outcomes [1–3]. Recent findings highlight the importance of detection of albuminuria and the clinical need to identify at risk individuals for regular screening [4,5]. Nevertheless, prevention of urinary albumin excretion and kidney disease progression is difficult to process in the early stage.

There is growing evidence that obesity and lipid abnormalities are important pathogenic mechanism in early deterioration of renal function [6,7]. Recently, we conducted clinical investigations to assess the associations of obesity measures and routine lipids parameters with albuminuria. Our data revealed that obesity measures including body mass index (BMI), waist circumference (WC) and body fat content were significantly correlated with increased urinary albumin excretion [8]. In another study from the same population, discordant associations of lipid parameters with albuminuria and renal insufficiency was detected, and triglyceride to high density lipoprotein cholesterol ratio (TG/HDL-C) is a better marker than other routine lipid measures for evaluating increased urinary albumin excretion [9]. Actually, the TG/HDL-C ratio has been reported to be correlated with CT measured visceral fat, which may be a simple and useful indicator for visceral obesity [10]. In

that study, however, no significant association of the TG/HDL-C ratio and subcutaneous fat was found.

Indeed, the distribution of fat tissue is rather crucial in light of the impact of obesity on systemic disease. It is noted that visceral fat accumulation and cytokines secreted by visceral adipose tissue are contributed to glomerular sclerosis and renal function damage [11,12]. On the basis of anthropometric (BMI and WC) and metabolic variables (TG and HDL-C), the visceral adiposity index (VAI) is a novel and accurate indicator to express both visceral fat distribution and adipose tissue dysfunction, which is significantly associated with many health-related outcomes in various populations [13–15]. We assumed that the influence of visceral fat content on the development of albuminuria is important, however, little was known about the relationship between VAI and albuminuria. Therefore, we explored the possible association between VAI level and increased urinary albumin excretion in the present study.

2. Subjects and methods

2.1. Study participants and design

A cross-sectional study was conducted in a community in Guangzhou, China from June to November, 2011. The study population was from the REACTION study and details of this study have been published previously [16–18]. At first, 10,104 subjects aged 40 years or older were invited to participate by examination notices or home visits during the recruiting phase. After this, 9916 subjects signed the consent form and participate in the survey. Those who failed to provided information (BMI: n = 206; WC: n = 62; TG: n = 23; HDL-C: n = 2; or urinary albumin-to-creatinine ratio [ACR]: n = 50) were excluded from the analyses. Accordingly, a total of 9473 eligible individuals were included in the final data analyses. The study protocol was approved by the Institutional Review Board of the Sun Yat-sen Memorial Hospital affiliated to Sun Yat-sen University and was in accordance with the principle of the Helsinki Declaration II. Written informed consent was obtained from each participant before data collection.

2.2. Data collection

Information on lifestyle factors, sociodemographic characteristics and family history were collected by using a standard questionnaire. Estimate physical activity was conducted by a short form of the International Physical Activity Questionnaire (IPAQ) [19]. Evaluation of total physical activity at leisure time was calculated by separate metabolic equivalent hours per week (MET-h/week). All participants completed measurements of blood pressure, body height and weight with the assistance of trained staff according to standard protocols. The average of three measurements of blood pressure was used for analysis. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Obesity was defined as BMI of 30.0 or higher and overweight was defined as BMI of 25.0–29.9 in the present study [20,21]. After at least 10 h overnight fasting, venous blood was collected for laboratory testing. Laboratory testing of TG, total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), γ-glutamyltransferase (γ-GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), fasting plasma glucose (FPG) and fasting serum insulin was finished by using an autoanalyser (Beckman CX-7 Biochemical Autoanalyser, Brea, CA, USA).

On the basis of data from Chinese chronic kidney disease patients, the Modification of Diet in Renal Disease (MDRD) equation was used to calculate estimated glomerular filtration rate (eGFR) expressed in mL/min per 1.73 m^2 using a formula of eGFR = 175 × [serum creatinine × 0.011]$^{-1.234}$ × [age]$^{-0.179}$ × [0.79

if female], where serum creatinine was expressed as μmol/L [22]. Metabolic syndrome was defined as the presence of any three of the following: 1. Serum TG concentration of 1.7 mmol/L or higher; 2. Serum HDL-C concentration of less than 1.0 mmol/L in men or less than 1.3 mmol/L in women; 3. Blood pressure of 130/85 mmHg or higher; 4. Plasma FPG concentration of higher than 5.6 mmol/L or drug treatment of elevated glucose; 5. WC equal to or higher than 85 cm in men and 80 cm in women [23]. According to the 1999 World Health Organization diagnostic criteria, diabetes was defined as the presence of one of the following: 1. A self-reported previously diagnosed diabetes by health care professionals; 2. Plasma FPG of 7.0 mmol/L or higher; 3. The 2-h oral glucose tolerance test plasma glucose level of 11.1 mmol/L or higher [24].

2.3. Definition of VAI and increased urinary albumin excretion

The VAI was determined by gender-specific equations and calculated using the following formulas. Males: [WC/(39.68 + (1.88 × BMI))] × (TG/1.03) × (1.31/HDL-C); Females: [WC/(36.58 + (1.89 × BMI))] × (TG/0.81) × (1.52/HDL-C) [13]. WC was calculated in cm and HDL-C and TG in mmol/L in the formula. First morning urine specimen collection was used for urinalysis if ACR level. The urinary albumin concentration and creatinine were determined by chemiluminescence immunoassay (Siemens Immulite 2000, United States) and a modified Jaffe method (Biobase-Crystal, Jinan, China) on the automatic analyzer, respectively. ACR was calculated by dividing the urinary albumin concentration in milligrams by the urinary creatinine concentration in grams. Abnormality in albumin excretion was defined according to the guideline from American Diabetes Association and increased urinary albumin excretion was defined as the ACR ranges 30 mg/g or higher [25].

2.4. Statistical analysis

Continuous variables were summarized by means ± standard deviation (SD) for normally distributed data or medians (interquartile ranges) for non-normally distributed data. All categorical parameters were expressed as numbers and proportions. Skewed distribution variables such as VAI, FPG, ALT, AST, γ-GGT TG and MET-h/week were logarithmically transformed before analysis. Linear regression analysis was fitted to test the trend of the demographic and other clinical characteristics across the quartiles of VAI groups. One-way ANOVA was used to compare among groups differences in clinical characteristics and laboratory variables, and post hoc comparisons was examined by using Bonferroni correction. The χ2 test was adopted to compare categorical variables.

Pearson's correlation coefficients of VAI with potential confounding factors for albuminuria were calculated except for those in the VAI calculating formula. Factors that were significant at P < 0.20 in Pearson's correlations were put into the multiple stepwise linear regression models to identify the independent determinants of VAI. Logistic regression analysis with unadjusted and multivariate-adjusted models was used to evaluate the association between VAI level and risk of prevalent increased urinary albumin excretion. Variables considered as potential covariates and significant in the stepwise linear regression were put into multivariate-adjusted logistic regression analysis. Model 1 is unadjusted. Model 2 is adjusted for age. Model 3 is adjusted for age, sex and BMI. Model 4 is adjusted for age, sex, BMI, current smoking and drinking status and physical activity. Model 5 is adjusted for age, sex, BMI, current smoking and drinking status, physical activity, systolic blood pressure (SBP), diastolic blood pressure (DBP), FPG, fasting insulin, LDL-C, γ-GGT and eGFR. Odds ratios (OR) with the corresponding 95% confidence intervals (95% CI) were

calculated. Subgroups analyses on the associations of VAI level with increased urinary albumin excretion were conducted with stratified factors including gender (men/women), age ($\geq$60/<60 years), degree of obesity (normal/overweight/obesity), hypertension (yes/no), metabolic syndrome (yes/no), diabetes (yes/no) and eGFR levels ($\geq$90; 60–89; <60 ml/min per 1.73 m^2). The interaction tests were conducted by including simultaneously the respective cross-product terms (strata variable multiplied by quartiles of VAI level), each strata factor and the quartiles of VAI level in the logistic regression analysis models.

Statistical analysis was performed using SAS version 9.3 (SAS Institute Inc, Cary, NC, USA). All statistical tests were two-sided, and a P value < 0.05 was considered statistically significant.

3. Results

3.1. Basic characteristics

The mean age was 55.9 $\pm$ 8.0 years among the 9473 enrolled individuals. The median VAI was 1.66 with interquartile range 1.09–2.65. There were 621 (6.6%) subjects categorized as increased urinary albumin excretion in the present study. The clinical and biochemical characteristics of the participants according to VAI quartiles were shown in Table 1. Subjects with increased VAI level had elevated age, BMI, WC, SBP, DBP, TG, TC, FPG, fasting insulin, ALT, γ - GGT and decreased HDL-C and eGFR levels in the study (all P for trend < 0.0001).

3.2. FLI and metabolic risk factors

Pearson's correlation revealed that age, physical activity level, SBP, DBP, FPG, fasting insulin, ALT, AST, γ-GGT and eGFR were significantly correlated with VAI level. The multivariable stepwise linear regression analysis demonstrated that SBP, DBP, LDL-C, FPG, fasting insulin, γ-GGT and eGFR were independent determinants for VAI (Table 2).

Table 2
Pearson's correlation and stepwise regression analysis of determinants of visceral adiposity index.

	r	P value	Standardized β	P value
Age (years)	0.08	<0.0001	–	–
Physical activity (MET-h/week)	−0.02	0.050	–	–
SBP (mmHg)	0.22	<0.0001	0.07	<0.0001
DBP (mmHg)	0.20	<0.0001	0.09	<0.0001
LDL-C (mmol/L)	−0.01	0.172	−0.04	0.0009
FPG (mmol/L)	0.20	<0.0001	0.11	<0.0001
Fasting insulin (μIU/ml)	0.32	<0.0001	0.25	<0.0001
ALT (U/L)	0.09	<0.0001	–	–
AST (U/L)	0.03	0.002	–	–
γ-GGT (U/L)	0.15	<0.0001	0.08	<0.0001
eGFR (ml/min per 1.73 m^2)	−0.07	<0.0001	−0.03	0.026

r, correlation coefficient; Standardized β, regression coefficient.

3.3. VAI and increased urinary albumin excretion

From the lowest quartile to the highest of VAI quartile, the prevalence of increased urinary albumin excretion was 4.5%, 6.9%, 8.9%, 8.7% in man and 2.9%, 5.1%, 6.8%, 10.6% in women (Fig. 1, P for trend = 0.0009 for man, P for trend < 0.0001 for women). Prevalent increased urinary albumin excretion tended to increase with the elevated VAI level in different eGFR strara (Table 3, P for trend < 0.0001 for eGFR $\geq$ 60 ml/min per 1.73 m^2, P for trend = 0.011 for eGFR < 60 ml/min per 1.73 m^2).

In the univariate logistic regression model, participants in quartile 2, quartile 3 and quartile 4 of VAI level, respectively, were more likely to have increased odds of increased urinary albumin excretion compared with those in the first quartile (Table 4, all P for trend < 0.0001). Stability of the result was confirmed by multivariate logistic regression analyses with different adjusted models. After adjusted for age, sex, BMI, current smoking status, current drinking status, physical activity, SBP, DBP, LDL-C, FPG, fasting insulin, γ-GGT and eGFR, compared with participants in the first quartile of VAI level, the odds of having increased urinary albumin

Table 1
Characteristics of study population according to visceral adiposity index quartiles.

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for trend
n (%)	2392 (25.3)	2343 (24.7)	2373 (25.1)	2365 (25.0)	
Visceral adiposity index	0.83 (0.68–0.96)	1.34 (1.21–1.50)*	2.05 (1.83–2.33)*	3.76 (3.11–5.29)*	<0.0001
Urinary albumin to creatinine ratio (mg/g)	7.43 (5.37–11.19)	7.93 (5.73–11.54)*	8.37 (5.84–12.51)*	8.89 (6.06–14.10)*	<0.0001
Age (years)	55.0 ± 7.9	55.6 ± 7.9*	56.0 ± 8.1*	56.9 ± 8.3*	<0.0001
Male [n (%)]	848 (35.5)	625 (26.7)	659 (27.8)	566 (23.9)	<0.0001
BMI (kg/m^2)	22.3 ± 3.4	23.3 ± 3.3*	24.2 ± 3.3*	24.8 ± 2.9*	<0.0001
WC (cm)	76.5 ± 8.4	80.6 ± 9.0*	83.6 ± 8.9*	86.0 ± 9.0*	<0.0001
SBP (mmHg)	121.4 ± 15.7	124.2 ± 15.8*	127.8 ± 16.0*	130.7 ± 16.6*	<0.0001
DBP (mmHg)	72.7 ± 9.8	74.3 ± 9.6*	76.4 ± 9.6*	77.8 ± 9.6*	<0.0001
Current smoking [n (%)]	243 (10.3)	226 (9.8)	232 (9.9)	233 (10.0)	0.759
Current drinking [n (%)]	97 (4.1)	74 (3.2)	67 (2.9)	74 (3.2)	0.057
TG (mmol/L)	0.80 (0.67–0.94)	1.10 (0.94–1.28)*	1.51 (1.27–1.77)*	2.42 (1.93–3.22)*	<0.0001
TC (mmol/L)	5.07 ± 1.12	5.13 ± 1.23	5.26 ± 1.28*	5.31 ± 1.32*	<0.0001
HDL-C (mmol/L)	1.60 ± 0.36	1.38 ± 0.31*	1.23 ± 0.28*	1.07 ± 0.25*	<0.0001
LDL-C (mmol/L)	2.99 ± 0.87	3.20 ± 0.95*	3.34 ± 0.98*	3.04 ± 0.99	0.0014
FPG (mmol/L)	5.27 (4.91–5.66)	5.36 (4.96–5.81)*	5.49 (5.05–6.02)*	5.63 (5.16–6.30)*	<0.0001
Fasting insulin (μIU/ml)	5.40 (4.10–7.10)	6.60 (5.00–8.80)*	7.90 (5.90–10.70)*	9.50 (7.10–12.60)*	<0.0001
ALT (U/L)	12.0 (9.0–17.0)	12.0 (9.0–16.0)	13.0 (9.0–18.0)*	14.0 (10.0–20.0)*	<0.0001
AST (U/L)	18.0 (15.0–22.0)	18.0 (15.0–21.0)*	18.0 (15.0–22.0)*	19.0 (15.0–23.0)	0.773
γ-GGT (U/L)	17.0 (13.0–23.0)	18.0 (14.0–26.0)*	21.0 (15.0–30.0)*	24.0 (17.0–35.0)*	<0.0001
eGFR (ml/min per 1.73 m^2)	102.4 ± 21.2	103.0 ± 23.3	102.0 ± 24.9	99.9 ± 24.6*	<0.0001
Physical activity (MET-h/week)	22.5 (10.5–49.0)	24.0 (10.5–49.0)	22.0 (10.5–42.0)	21.0 (10.5–42.0)	0.021

Data were means ± SD or medians (interquartile ranges) for skewed variables or numbers (proportions) for categorical variables.
P for trend was calculated for the linear regression analysis tests across the groups. P values were for the ANOVA or χ^2 analyses across the groups.
*P < 0.05 compared with Quartile 1 of visceral adiposity index.
BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; γ-GGT, γ-glutamyltransferase.
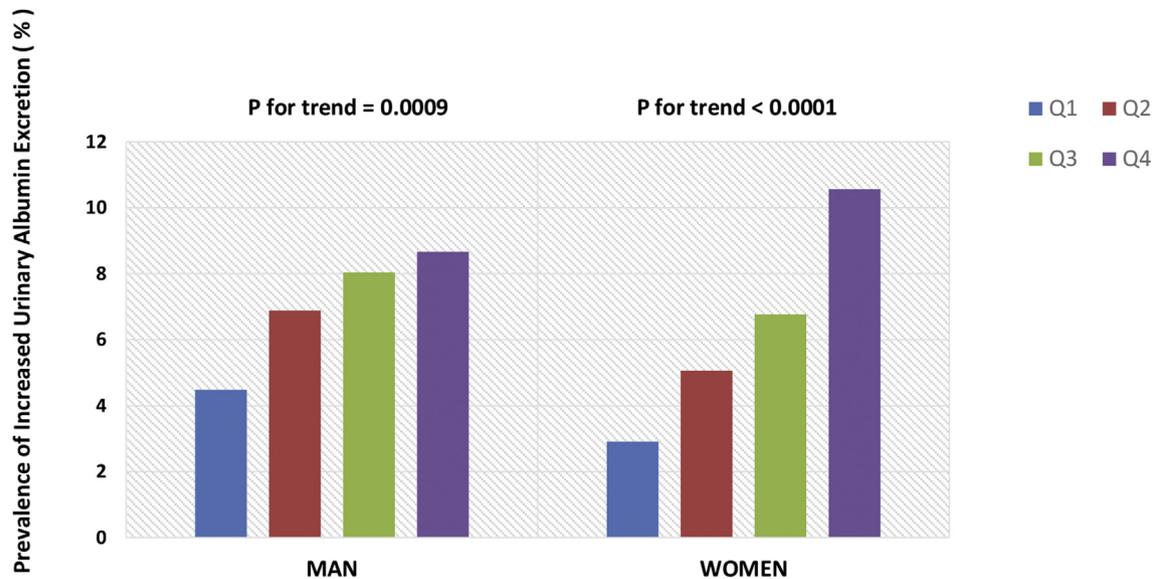
Fig. 1. Prevalence of increased urinary albumin excretion in different quartiles of visceral adiposity index levels.

Table 3
Prevalence of increased urinary albumin excretion in different quartiles of visceral adiposity index by eGFR levels.

	Prevalence of increased urinary albumin excretion (%)				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for trend
eGFR* ≥ 90 (ml/min per 1.73 m²)	3.1	4.9	6.0	8.5	<0.0001
90 > eGFR ≥ 60 (ml/min per 1.73 m²)	3.9	7.0	8.3	12.0	<0.0001
eGFR < 60 (ml/min per 1.73 m²)	13.9	15.8	34.0	33.3	0.011

*eGFR, estimated glomerular filtration rate.

Table 4
The risk of prevalent increased urinary albumin excretion according to quartiles of visceral adiposity index.

		Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for trend
Increased urinary albumin excretion	Model 1	1	1.63 (1.23–2.17)	2.13 (1.63–2.79)	3.13 (2.42–4.04)	<0.0001
	Model 2	1	1.61 (1.21–2.13)	2.07 (1.58–2.71)	2.97 (2.30–3.85)	<0.0001
	Model 3	1	1.52 (1.14–2.01)	1.85 (1.41–2.43)	2.59 (1.99–3.37)	<0.0001
	Model 4	1	1.36 (1.01–1.85)	1.73 (1.29–2.32)	2.39 (1.80–3.17)	<0.0001
	Model 5	1	1.29 (0.94–1.76)	1.46 (1.08–1.97)	1.79 (1.33–2.41)	<0.0001

Data are odds ratios (95% confidence interval). Participants without increased urinary albumin excretion are defined as 0 and with increased urinary albumin excretion as 1.
Model 1 is unadjusted.
Model 2 is adjusted for age.
Model 3 is further adjusted for sex, BMI.
Model 4 is further adjusted for current smoking status, current drinking status, physical activity.
Model 5 is further adjusted for SBP, DBP, LDL-C, FPG, fasting insulin, γ-GGT and eGFR.

excretion was higher for those in the third VAI quartile (adjusted odds ratio, 1.46 [95% CI, 1.08 to 1.97]) and fourth VAI quartile (adjusted odds ratio, 1.79 [95% CI, 1.33 to 2.41]).

3.4. Subgroup analysis

In subgroups analyses, the associations of VAI level with increased urinary albumin excretion were not consistently the same (Fig. 2). Significant relationship of VAI level with increased urinary albumin excretion was detected in women, younger subjects, normal and overweight subjects, non-diabetes subjects and those with eGFR ≥60 ml/min per 1.73 m² (all P < 0.05). Interactions between quartiles of VAI and stratified factors was significant in sexual stratification, which bring us closer to understanding the gender-specific interactions between visceral fat distribution and albuminuria.

4. Discussion

Determine early warning parameters for urinary albumin excretion in kidney disease is of great importance [26]. As one of the applicable index representing visceral adiposity in clinical practice, VAI is associated with deterioration of renal function based on previous publications. By including 23,570 subjects aged 18 years or older, a recent cross-sectional study conducted by Chen and colleagues reporting the relationship between VAI and prevalence of CKD [27]. In the study, a higher VAI was associated with increased risk of prevalent CKD. However, CKD was defined only by the eGFR levels and albuminuria was not evaluated in that study. Moreover, subjects from the study were underwent annual heath checkups and without significant comorbidities. Therefore, their results are only representative of relatively healthy adults. Using decreased eGFR or the presence of albuminuria to define CKD, a
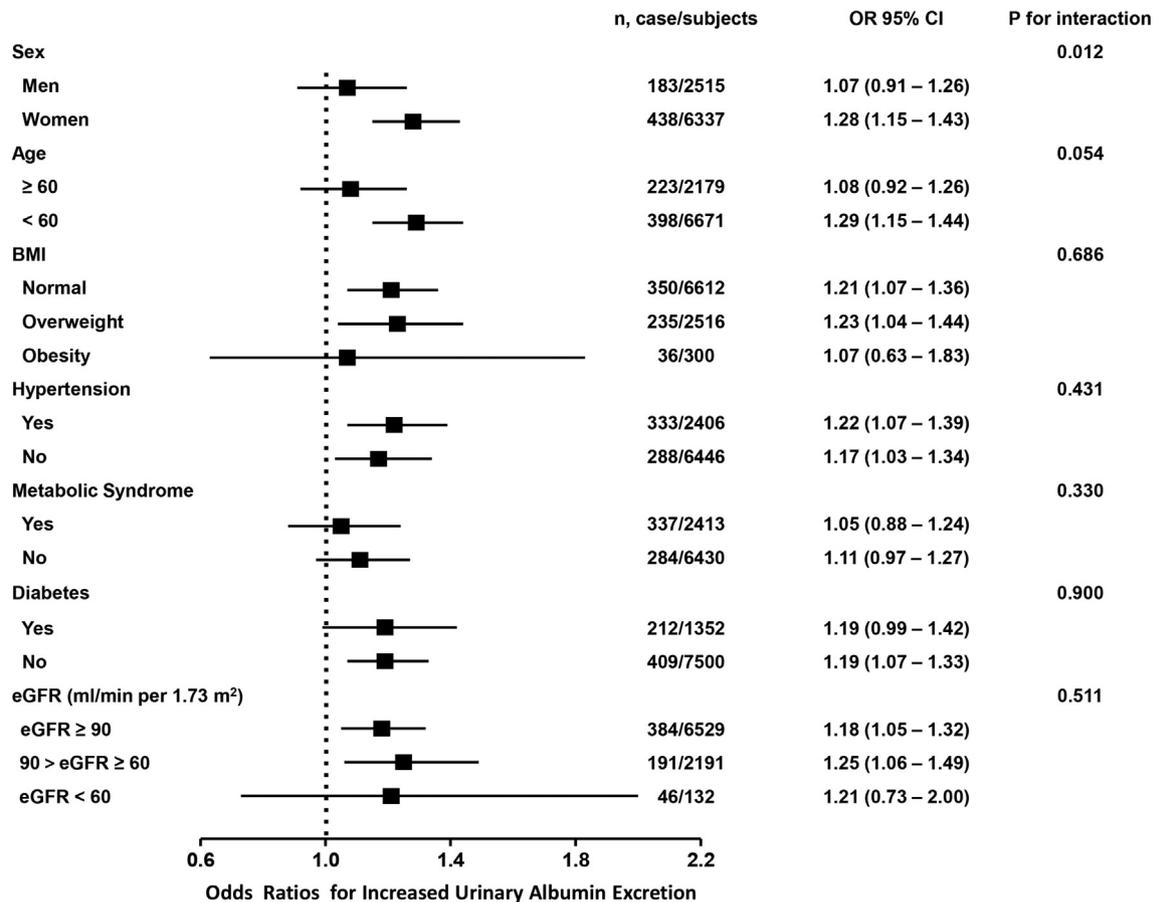
	n, case/subjects	OR 95% CI	P for interaction
Sex			0.012
Men	183/2515	1.07 (0.91 – 1.26)	
Women	438/6337	1.28 (1.15 – 1.43)	
Age			0.054
≥ 60	223/2179	1.08 (0.92 – 1.26)	
< 60	398/6671	1.29 (1.15 – 1.44)	
BMI			0.686
Normal	350/6612	1.21 (1.07 – 1.36)	
Overweight	235/2516	1.23 (1.04 – 1.44)	
Obesity	36/300	1.07 (0.63 – 1.83)	
Hypertension			0.431
Yes	333/2406	1.22 (1.07 – 1.39)	
No	288/6446	1.17 (1.03 – 1.34)	
Metabolic Syndrome			0.330
Yes	337/2413	1.05 (0.88 – 1.24)	
No	284/6430	1.11 (0.97 – 1.27)	
Diabetes			0.900
Yes	212/1352	1.19 (0.99 – 1.42)	
No	409/7500	1.19 (1.07 – 1.33)	
eGFR (ml/min per 1.73 m^2)			0.511
eGFR ≥ 90	384/6529	1.18 (1.05 – 1.32)	
90 > eGFR ≥ 60	191/2191	1.25 (1.06 – 1.49)	
eGFR < 60	46/132	1.21 (0.73 – 2.00)	

Odds Ratios for Increased Urinary Albumin Excretion

Fig. 2. Prevalence of increased urinary albumin excretion with each quartile increase of visceral adiposity index in different subgroups.

recent study conducted in 2142 Chinese subjects confirmed that the VAI is a useful clinical indicators of CKD [28]. Nevertheless, one limitation of the study is that they did not analyze the exact association of VAI with albuminuria as separate entity. Recently, a relative small sample size study found that VAI is positively correlated with ACR and prevalent CKD in 1581 residents aged over 40 years [29]. However, such association was not significant after adjustment of FPG and blood pressure levels. Because of the inconsistent results and the possibility of sampling bias, as well as the unstable character of spot urine sample of these cohorts, the rationality and practicality of the results of these studies should be verified.

By including 9473 Chinese subjects from the REACTION study, we found that deposition of visceral fat assessed by VAI was associated with increased urinary albumin excretion independent of potential confounding risk factors. To our current knowledge, this is the largest population-based study to explore the association of VAI with increased urinary albumin excretion. Early intervention is important for albuminuria while improve the abnormal fat distribution might be helpful for prevention and early detection of this unhealthy status.

Indeed, WC having been considered the most valid clinical parameter of regional distribution of adipose tissue. Nevertheless, WC alone does not help in distinguishing between visceral and subcutaneous fat mass in the abdominal region [30]. Magnetic resonance imaging (MRI) and computed tomography (CT) are the gold standard for determining the extent of visceral fat area according to the consensus statement from the International Diabetes Federation [31]. However, these imaging techniques are unsuitable for routine clinical practices in a general population due to availability, time-consuming, expense, and radiologic hazard. Therefore, an effective, convenient and relatively accurate process for the for the evaluation of visceral fat mass is desperately needed [32]. As a mathematical model that includes anthropometric and metabolic parameters, VAI is closely correlated with MRI-measured visceral adiposity, which is a useful indicator of adipose distribution that independently correlated with cardio-metabolic risk and cerebro-vascular events [13,33]. Albuminuria can predict various micro- and macro-vascular complications related to visceral fat adiposity. To enhance the value of VAI as a predictive tool for metabolic and vascular diseases, our study supplemented and confirmed the association between the VAI and increased urinary albumin excretion in a general population.

Several limitations of the present study should be acknowledged. Firstly, by including only Chinese subjects, our results might not be representative of other ethnic groups, especially for those in the developed or undeveloped countries. To some extent, the population in the present study was still a convenience sample and selection bias is inevitable. Secondly, owing to the nature of observational design of the current study, we should cautiously interpret the present findings as no causal inference can be drawn. Further prospective studies that allow us to evaluate the predictive power of the VAI regarding albuminuria risk is needed. Thirdly, we observed that VAI play a different efficiency for elevated urinary excretion between genders. Significant association of VAI with increased urinary albumin excretion was only detected in women. Based on the further analysis, the interaction between VAI and sex may represent one of the fundamental effect of increased urinary

albumin excretion. Actually, most women in the present study are in the perimenopausal or postmenopausal stage. The decrease in production of estrogen and progesterone during the menopausal transition is a special period in a woman's life and the impact may reach far beyond the reproductive system [18,34]. In this particular physiological stages, fat redistribution occurs due to the radically changing sex hormones. Accordingly, excessive accumulation of visceral adipose tissue during this phase will lead to inflammatory processes and glomerular structures injury in women [35]. Nevertheless, more evidence is needed to illuminate the sexual difference in VAI regarding its practical ability in albuminuria. Fourthly, in subgroups analyses, the associations of VAI level with albuminuria were not consistently the same while positive but not significant associations of VAI level with albuminuria were detected in older age, obese and metabolic syndrome subgroups. In interaction analysis, however, no statistically significance of interaction term between VAI and these strata factors were found. We speculated that older subjects or those with obese and metabolic syndrome were inclined to change the diet structure and received related treatment, which may be beneficial to their albuminuria. Nevertheless, to strengthen the findings of the present study, individual quantification of lifestyle factors and detailed medical records should also be evaluated when analyzing possible risk factors associated with albuminuria. Missing of these data may influence risk estimates and result interpreting in this setting.

5. Conclusion

The present study demonstrates that elevated VAI level is independently associated with prevalent increased urinary albumin excretion. Findings of the current study highlights the importance of paying clinical attention to albuminuria in patients with visceral adipose accumulation. Further prospective studies are necessary to verify our findings in external populations.

The author contribution lists

Conceived and designed the experiments: Y. L. and K. S.; Performed the experiments: F. L., Y. Q., W. F., K. S. and D. L.; Analyzed the data: K. S. and M. R.; Wrote the manuscript: K.S. and D. L.

Statement of authorship

All authors have read and agree to the paper as written. The work has not been published previously, and not under consideration for publication elsewhere.

Data sharing statement

Main document data and additional unpublished data from the study are available by sending Email to lizyhenu@163.com with proper purposes.

Conflict of interest

The authors have declared that no competing interests exist.

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