A novel index, Chinese visceral adiposity index is closely associated with urinary albumin-creatinine ratio in Chinese community adults, especially in hypertensive or hyperglycemic population: Results from the REACTION study

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Abstract

Background: The association between the Chinese Visceral Adiposity Index (CVAI) and urinary albumin to creatinine ratio (UACR) has not been illustrated. The current study aimed to investigate the association between CVAI and UACR and to compare the discriminative power of CVAI, triglyceride, body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR) with UACR in the Chinese community population.

Methods: This study included 34,732 participants from the REACTION (Risk Evaluation of cAncers in Chinese diabeTic Individuals) study. Binary logistic regression analyses were performed to detect the association between CVAI, triglyceride, BMI, WC, WHR and UACR.

Results: Binary logistic regression analysis showed that, after adjusting for potential confounders, in women, CVAI (odds ratio [OR]: 1.16, 95% confidence interval [CI]: 1.01–1.34) and triglyceride (OR: 1.18, 95% CI: 1.04–1.33) were highly associated with UACR.
associated with UACR, whereas BMI, WC, and WHR were not associated with UACR; in men, CVAI (OR: 1.24, 95% CI: 1.02–1.50), WC (OR: 1.21, 95% CI 1.00–1.48), and triglycerides (OR: 1.18, 95% CI 0.97–1.44) were associated with UACR, whereas BMI and WHR were not associated with UACR. Stratified analysis showed that the correlation between CVAI and UACR was stronger in the population with $5.6 \leq$ fasting blood glucose (FBG) $<7.0$ or $7.8 \leq$ post-load blood glucose (PBG) $<11.1$ mmol/L, FBG $\geq 7.0$ or PBG $\geq 11.1$, systolic blood pressure $\geq 140$ mmHg or diastolic blood pressure $\geq 90$ mmHg.

Conclusions: In the Chinese general population, CVAI and UACR were significantly associated in both genders. At higher CVAI levels, the population with prediabetes, diabetes, and hypertension has a more significant association between CVAI and UACR.

KEYWORDS
Chinese Visceral Adiposity Index, diabetic complications, diabetic nephropathy, obesity, urinary albumin to creatinine ratio

Highlights
• This is the first large-sample, multicenter study of the relationship between Chinese Visceral Adiposity Index (CVAI) and urinary albumin to creatinine ratio (UACR) in Chinese community adults.
• CVAI and UACR were significantly associated in both genders.
• At higher CVAI levels, the population with prediabetes, diabetes, and hypertension has a more significant correlation between CVAI and UACR.

1 INTRODUCTION

Microalbuminuria is the inchoate symbol of diabetic nephropathy and is closely related to cardiovascular disease (CVD), cardiovascular mortality and all-cause mortality. The LIFE and PREVEND investigations found a significant correlation between increasing urine albumin excretion and ischemic CVD morbidity and death. In the general population, the occurrence of microalbuminuria is a sign of diabetes, hypertension, and CVD. A high urinary albumin creatinine ratio (UACR) is not only a symbol of kidney dysfunction but also indicates a higher risk of CVD. Every 3.01 mg/g rise in UACR contributed to a 5.9% increase of CVD incidents. UACR elevated within the accepted normal range is linked to an increased risk of CVD, as well as an increased risk of the cardiovascular death rate. Nonetheless, because preventing urinary albumin excretion and renal dysfunction progression is hard in the early phase, identifying early warning signs for albuminuria is essential.

The correlation between obesity and renal dysfunction was first noted in 1974, and obesity was found to be highly correlated with albuminuria. Numerous studies in recent years have demonstrated that visceral adiposity, rather than subcutaneous adiposity or total adiposity, is closely related to an increase in albuminuria. The gold standard for evaluating fat accumulation is magnetic resonance imaging and computed tomography (CT). However, given the availability, time involved, expense, and radiologic risk, these imaging technologies are inappropriate for regular clinical examine among the general population. Therefore, a practical, user-friendly, and relatively accurate method for evaluating visceral adiposity mass is urgently required.

Traditional anthropometric measures, such as body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR), have the general disadvantage that they do not take into account metabolic indicators and they could not accurately assess visceral adiposity. Chinese Visceral Adiposity Index (CVAI) is a novel visceral fat indication developed specifically for Asian people depending on age, BMI, WC, and metabolic parameters. A total of 485 participants from Xiamen, China received abdominal CT for visceral adiposity area, then CVAI was established utilizing multivariate linear regression analyses and was further verified in 6495 participants from Shanghai, China that it was highly correlated with visceral adipose and it was more valuable compared to BMI.
and WC in the assessment of metabolic risks.\textsuperscript{19} Besides, CVAI has been reported to be more significantly related to diabetes,\textsuperscript{20} diabetes complications,\textsuperscript{21} atherosclerosis,\textsuperscript{22,23} polycystic ovary syndrome,\textsuperscript{24} hypothyroidism,\textsuperscript{25} and hypertension\textsuperscript{26} than other obesity indices among the Chinese population, and one study has discovered a close relation between CVAI and diabetes among the Japanese population.\textsuperscript{27} However, the research on the relationship between CVAI and UACR is limited. Therefore, the present study aimed to explore the relationship between CVAI and UACR and compare the discriminative power of CVAI and traditional indicators for UACR in Chinese community adults.

2 | METHODS

2.1 | Study subjects

An ongoing cohort study named REACTION (Risk Evaluation of cAncers in Chinese diabeTic Individuals)\textsuperscript{28} designed to research the correlation of diabetes and prediabetes with the risk of cancer in the Chinese population was performed based on the community. The REACTION study is a multicenter, prospective observational study, in which participants have proof of local household registration and be at least 40 years of age, and there is no gender or ethnicity restriction. The present study population came from 7 centers of the REACTION study; 47,808 participants were investigated between March and December 2012. After excluding the corresponding participants according to the exclusion criteria, 34,732 study subjects were enrolled. The exclusion criteria are as follows: (1) suffer from renal disease; (2) use of angiotensin-converting enzyme inhibitors or angiotensin receptor blocker medicines; (3) use of lipid-lowering medications; and (4) lack of important information or essential test results.

2.2 | Questionnaire survey

The participants’ essential information was acquired through a standardized questionnaire. The investigators have been professionally trained. The questionnaire broadly covers year of birth, medical history, current medication status, smoking and drinking habits, marriage status, education level, occupation, and other important information.

2.3 | Physical examination

The height, weight, hip circumference, and WC were measured and documented. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by the same investigator three times, 5 min apart. The mean values of these three measurements were used in statistical analysis.

2.4 | Lab measurements

The collection of blood samples was at 8–9 am after 8–10 h of overnight fasting. The following important indicators were measured and documented: (1) total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides; (2) fasting blood glucose (FBG), 2 h post-load blood glucose (PGB), and hemoglobin A1c (HbA1c); (3) serum creatinine (Scr), aspartate transferase (AST), and alanine transferase (ALT); and (4) other biochemical indexes.

Participants without or with diabetes underwent 75 g oral glucose tolerance or 100 g steamed-bread meal, separately.

Morning urine samples were collected, and urine albumin and creatinine concentrations were determined.

2.5 | Calculation of UACR, CVAI, BMI, WHR, and estimated glomerular filtration rate (eGFR)

(1) UACR was calculated through dividing the urinary albumin by the urinary creatinine; (2) BMI was expressed in kg/m\textsuperscript{2}, BMI = weight (Kg) ÷ height\textsuperscript{2} (m); (3) WHR = WC ÷ hip circumference; (4) eGFR was expressed in ml/min per 1.73 m\textsuperscript{2}, eGFR = 175 × (Scr in mg/dl) \(–1.154 \times \text{age} – 0.203 \times (0.742 \text{ for women}) \times (1.212 \text{ if African American})

(5) the CVAI were calculated according to gender as follows:

- Males: CVAI = \(-267.93 + 0.68 \times \text{age(y)} + 0.03 \times \text{BMI (kg/m}^2\text{)} + 4.00 \times \text{WC (cm)} + 22.00 \times \text{Lg triglyceride (mmol/L)} - 16.32 \times \text{HDL-C (mmol/L)}\)

- Females: CVAI = \(-187.32 + 1.71 \times \text{age(y)} + 4.32 \times \text{BMI (kg/m}^2\text{)} + 1.12 \times \text{WC (cm)} + 39.76 \times \text{Lg triglyceride (mmol/L)} - 11.66 \times \text{HDL-C (mmol/L)}\)

2.6 | Definition

CVAI, WC, WHR, BMI, and triglyceride were divided into four groups: the <25% group (the control group), the 25–50% group, the 50–75% group, and the ≥75% group, according to quartile division of the subjects and conducted separately by gender (Table 1). We selected only one lipid, triglyceride, to compare its prediction ability
with other obesity indicators for UACR, because previous studies have shown that triglyceride, but not total cholesterol, HDL-C, or LDL-C, is significantly associated with UACR. Increased albuminuria was defined as UACR ≥ 30 mg/g, indicating renal dysfunction. Thus, UACR was divided into two groups: normal group: <30 mg/g and increased albuminuria group: UACR ≥ 30 mg/g.

### 2.7 Statistical analysis

SPSS 24.0 (IBM) was used for the statistical analysis. Continuous variables were shown as mean ± SD. Categorical variables were shown numerically (proportionally). Differences in continuous variables between the two groups of UACR were compared using the Kruskal–Wallis test, and categorical variables were analyzed using the chi-square test. Binary logistic regression was used to test the associations of CVAI, WC, WHR, BMI, and triglyceride with UACR and was conducted separately by gender. Adjustment variables were tested by collinearity diagnosis according to the following criteria: variance inflation factor > 10 or tolerance near 0.1; condition index > 30; and variance proportions > 50%. The adjusted variables had the following criteria: (1) there was a significant difference between the UACR < 30 mg/g group and the UACR ≥ 30 mg/g group in both genders; and (2) there was no collinearity. Model 1 was adjusted for age and center. Model 2: Model 1 + occupation, current drinking habits, and CVD history. Model 3: Model 2 + ALT, GGT, eGFR, and total cholesterol. Model 4: Model 3 + SBP and DBP. Model 5: Model 4 + HbA1c, FBG, and PBG.

After controlling confounders in model 5, the association between independent variables and CVAI was explored within subgroups of blood pressure and blood glucose.

All statistical tests were two sided, and \( p < .05 \) was considered statistically significant.

### 3 | RESULTS

#### 3.1 Clinical characteristics of the study population

The current study included 34,732 participants (Table 2), with 10,494 (30.2%) males and 24,238 (69.8%) females, and their median age (Q1–Q3) was 57.33 (52.18–65.58). Participants (both male and female) with increased UACR had increased age, CVAI, BMI, WC, triglyceride, ALT, GGT, FBG, PBG, HbA1c, SBP, and DBP, as well as decreased HDL-C and eGFR. The prevalence of CVD events (myocardial infarction, stroke, and coronary heart disease) was higher in both male and female participants with increased UACR.

#### 3.2 The association between CVAI and increased UACR in the male subjects

Table 3 shows the association between variables and increased UACR (UACR ≥ 30 mg/g) in male subjects. In model 5, after adjusting for all confounders, CVAI (Q4: odds ratio [OR]: 1.24, 95% confidence interval [CI]: 1.02–1.50), WC (Q4: OR: 1.21, 95% CI: 1.00–1.48) and triglyceride (Q4: OR: 1.18, 95% CI: 0.97–1.44) were significantly correlated with UACR, whereas WHR (Q4: OR: 1.06, 95% CI: 0.88–1.28) and BMI (Q4: OR: 1.10, 95% CI: 0.91–1.33) were uncorrelated with UACR.

#### 3.3 The association between CVAI and increased UACR in the female subjects

In model 5 (Table 4), after adjusting for all confounders, only triglyceride (Q4: OR: 1.18, 95% CI: 1.04–1.33) and CVAI (Q4: OR: 1.16, 95% CI: 1.01–1.34) were significantly correlated with UACR, however, WC (Q4: OR: 1.07, 95% CI: 0.95–1.21), WHR (Q4: OR: 0.94, 95% CI: 0.84–1.07), BMI (Q4: OR: 1.05, 95% CI: 0.94–1.18), and UACR were not correlated.

#### 3.4 Stratification analysis

In Table 5, in male or female normotensive participants, CVAI, BMI, WC, WHR, and triglycerides were not associated with UACR. In male hypertensive participants, CVAI (Q4: OR: 1.54, 95% CI: 1.17–2.01), BMI (Q4: OR: 1.33, 95% CI: 1.03–1.72), WC (Q4: OR: 1.43, 95% CI: 1.10–1.85), and triglycerides (Q4: OR: 1.30, 95% CI: 1.01–1.67) were significantly associated with UACR, whereas WHR (Q4: OR: 1.20, 95% CI: 0.94–1.54) was not associated with
| Variable            | Total                  | Male                      | Female                   |
|---------------------|------------------------|---------------------------|--------------------------|
|                     | Number                 | UACR <30 mg/g             | UACR ≥30 mg/g            | UACR <30 mg/g             | UACR ≥30 mg/g             |
|                     | 34 732                 | 9238                      | 1256                     | 20 666                    | 3572                      |
| Age, years          | 57.33 (52.18, 65.58)   | 59.17 (53.75, 65.14)      | 62.47 (55.79, 70.18)***  | 56.05 (51.35, 61.54)      | 59.95 (53.80, 68.06)***   |
| CVAI                | 104.31 (78.70, 131.42) | 114.47 (86.19, 141.44)    | 127.26 (99.49, 155.40)***| 97.89 (74.04, 123.14)     | 114.07 (87.56, 139.72)*** |
| BMI, Kg/m²          | 24.30 (22.15, 26.61)   | 24.51 (22.49, 26.71)      | 25.05 (22.86, 27.36)***  | 24.09 (21.96, 26.44)      | 24.45 (22.25, 27.02)***   |
| WC, cm              | 86.00 (80.00, 93.00)   | 89.00 (83.00, 95.0)       | 91.00 (85.00, 98.00)***  | 84.00 (78.00, 90.33)      | 86.00 (80.00, 93.00)***   |
| WHR                 | 0.89 (0.84, 0.93)      | 0.91 (0.88, 0.95)         | 0.92 (0.89, 0.95)***     | 0.87 (0.83, 0.92)         | 0.88 (0.84, 0.93)***      |
| LDL-C, mmol/L       | 2.94 (2.36, 3.55)      | 2.83 (2.29, 3.41)         | 2.74 (2.15, 3.33)***     | 3.02 (2.43, 3.46)         | 3.12 (2.53, 3.46)***      |
| HDL-C, mmol/L       | 1.29 (1.09, 1.52)      | 1.17 (1.00, 1.37)         | 1.11 (0.95, 1.32)***     | 1.36 (1.16, 1.58)         | 1.28 (1.10, 1.50)***      |
| TC, mmol/L          | 5.05 (4.33, 5.78)      | 4.79 (4.13, 5.48)         | 4.70 (4.01, 5.44)***     | 5.18 (4.46, 5.92)         | 5.06 (4.33, 5.78)***      |
| Triglyceride, mmol/L| 1.37 (0.98, 1.97)      | 1.38 (0.98, 2.04)         | 1.56 (1.07, 2.33)***     | 1.32 (0.96, 1.89)         | 1.56 (1.11, 2.22)***      |
| ALT, U/L            | 15.00 (11.00, 21.00)   | 16.00 (12.00, 23.00)      | 17.00 (12.00, 25.00)***  | 14.00 (11.00, 20.00)      | 15.00 (11.00, 21.00)***   |
| AST, U/L            | 20.00 (17.00, 25.00)   | 21.00 (17.00, 25.00)      | 21.00 (17.00, 27.00)***  | 20.00 (17.00, 24.00)      | 21.00 (17.00, 26.00)***   |
| GGT, U/L            | 21.00 (15.00, 32.00)   | 26.00 (18.00, 39.00)      | 28.00 (19.00, 45.00)***  | 19.00 (14.00, 27.00)      | 20.00 (15.00, 31.00)***   |
| eGFR, ml/(min/1.73 m²)| 89.79 (80.15100.63)   | 95.66 (82.62106.93)       | 90.08 (75.62103.04)***  | 88.81 (80.29, 98.01)      | 85.68 (76.42, 95.61)***   |
| FBG, mmol/L         | 5.53 (5.10, 6.17)      | 5.64 (5.18, 6.37)         | 6.19 (5.38, 7.97)***     | 5.46 (5.08, 5.99)         | 5.66 (5.17, 6.57)***      |
| PBG, mmol/L         | 7.39 (6.02, 9.68)      | 7.54 (6.00, 10.09)        | 9.30 (6.80, 13.92)***    | 7.18 (5.98, 9.11)         | 8.20 (6.45, 11.29)***     |
| HbA1c, %            | 5.90 (5.60, 6.30)      | 5.90 (5.60, 6.30)         | 5.90 (5.60, 6.20)        | 5.90 (5.60, 6.20)         | 5.90 (5.60, 6.50)***      |
| SBP, mmHg           | 129.33 (117.00, 144.00)| 131.00 (119.33, 144.33)   | 141.33 (125.00, 156.92)***| 127.00 (115.33, 141.00)   | 136.33 (120.67, 152.33)***|
| DBP, mmHg           | 76.67 (70.00, 84.00)   | 79.00 (72.00, 86.00)      | 81.00 (74.00, 90.07)***  | 75.33 (68.67, 82.08)      | 77.67 (70.33, 85.33)***   |
| Drinking, (%)       |                        |                           |                          |                          |                          |
| Never               | 26 118 (75.2)          | 4431 (48.0)               | 676 (53.8)***            | 17 812 (86.2)             | 3199 (89.6)***            |
| Occasional          | 6332 (18.2)            | 3033 (32.8)               | 354 (28.2)***            | 2612 (12.6)               | 333 (9.3)***              |
| Frequently          | 2282 (6.6)             | 1774 (19.2)               | 226 (18.0)***            | 242 (1.2)                 | 40 (1.1)***               |
| Smoking, (%)        |                        |                           |                          |                          |                          |
| Never               | 29 835 (85.9)          | 5331 (57.7)               | 729 (58.0)               | 20 275 (98.1)             | 3500 (98.0)               |
| Occasional          | 778 (2.2)              | 528 (5.7)                 | 71 (5.7)                 | 157 (0.8)                 | 22 (0.6)                  |
| Frequently          | 4119 (11.9)            | 3379 (36.6)               | 456 (36.3)               | 234 (1.1)                 | 50 (1.4)                  |
| CVD (%)             |                        |                           |                          |                          |                          |
| Yes                 | 1657 (4.8)             | 466 (5.0)                 | 113 (9.0)***             | 827 (4.0)                 | 251 (7.0)***              |
| No                  | 33 075 (95.2)          | 8772 (95.0)               | 1143 (91.0)***           | 19 839 (96.0)             | 3321 (93.0)***            |
| Married/cohabitating (%) |                    |                           |                          |                          |                          |
| Yes                 | 30 691 (88.4)          | 8721 (94.4)               | 1159 (92.3)              | 17 918 (86.7)             | 2893 (81.0)***            |
| No                  | 4041 (11.6)            | 517 (5.6)                 | 97 (7.7)                 | 2748 (13.3)               | 679 (19.0)***             |
UACR. In female hypertensive participants, CVAI (Q4: OR: 1.41, 95% CI: 1.12–1.78), triglycerides (Q4: OR: 1.32, 95% CI: 1.11–1.58), and WC (Q4: OR: 1.25, 95% CI: 1.04–1.49) were significantly associated with UACR, whereas BMI (Q4: OR: 1.15, 95% CI: 0.97–1.36) and WHR (Q4: OR: 1.03, 95% CI: 0.86–1.23) were not associated with UACR.

In Table 6, in male normoglycemic participants, CVAI, BMI, WC, WHR, and triglycerides were not associated with UACR. Among female normoglycemic participants, only triglycerides were significantly associated with UACR, whereas CVAI, BMI, WC, and WHR were not correlated with UACR. In male hyperglycemic participants, CVAI (Q4: OR: 1.37, 95% CI: 1.10–1.72) and WC (Q4: OR: 1.32, 95% CI: 1.04–1.68) were significantly associated with UACR, whereas BMI (Q4: OR: 1.13, 95% CI: 0.90–1.43), WHR (Q4: OR: 1.19, 95% CI: 0.95–1.49), and triglycerides (Q4: OR: 1.27, 95% CI: 0.99–1.62) were not. In female hyperglycemic participants, CVAI (Q4: OR: 1.38, 95% CI: 1.15–1.66), BMI (Q4: OR: 1.18, 95% CI: 1.01–1.38), and WC (Q4: OR: 1.27, 95% CI: 1.08–1.50) were significantly associated with UACR, whereas WHR (Q4: OR: 1.13, 95% CI: 0.96–1.32) and triglycerides (Q4: OR: 1.13, 95% CI: 0.95–1.33) were not.

**4 | DISCUSSION**

As far as we know, this is the first study to explore the relationship between CVAI and UACR in a large sample, multicenter Chinese general population. The principal discoveries of this study indicated that CVAI was significantly associated with increased UACR in male and female Chinese community adults. In men, CVAI and WC had similar ability to discriminate albuminuria, and they were stronger than BMI, WHR, and triglycerides in discriminating albuminuria. In women, CVAI and triglycerides had similar ability to discriminate albuminuria, and they were stronger than BMI, WHR, and WC in discriminating albuminuria. Besides, CVAI was more strongly associated with elevated UACR than traditional indicators of obesity and triglycerides in men or women with hypertension or hyperglycemia. Therefore, for people with hypertension or hyperglycemia, it is important to monitor CVAI and prevent albuminuria in time.

A robust body of literature has uncovered that visceral obesity is highly associated with renal dysfunction and microalbuminuria. Chung’s study suggested that patients with type 2 diabetes who had more visceral adipose were more likely to develop diabetic nephropathy. A research by Framingham Heart Study reported that
| Variable | Module 0 OR (95% CI) | Module 1 OR (95% CI) | Module 2 OR (95% CI) | Module 3 OR (95% CI) | Module 4 OR (95% CI) | Module 5 OR (95% CI) |
|----------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| CVAI     |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.17 (0.97, 1.41)    | 1.07 (0.89, 1.30)    | 1.07 (0.88, 1.29)    | 1.00 (0.83, 1.21)    | 0.90 (0.74, 1.09)    | 0.86 (0.70, 1.04)    |
| Q3       | **1.40 (1.17, 1.67)** | **1.25 (1.04, 1.51)** | **1.26 (1.04, 1.51)** | 1.14 (0.95, 1.38)    | 0.98 (0.81, 1.18)    | 0.89 (0.73, 1.08)    |
| Q4       | **2.16 (1.82, 2.55)** | **1.95 (1.63, 2.33)** | **1.93 (1.61, 2.31)** | **1.71 (1.42, 2.06)** | **1.38 (1.15, 1.67)** | **1.24 (1.02, 1.50)** |
| WHR      |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.13 (0.94, 1.34)    | 1.11 (0.92, 1.32)    | 1.10 (0.92, 1.32)    | 1.06 (0.89, 1.28)    | 0.98 (0.81, 1.17)    | 0.94 (0.78, 1.13)    |
| Q3       | **1.25 (1.05, 1.48)** | **1.26 (1.05, 1.51)** | **1.25 (1.05, 1.50)** | 1.16 (0.97, 1.39)    | 1.03 (0.85, 1.25)    | 0.92 (0.77, 1.11)    |
| Q4       | **1.50 (1.27, 1.77)** | **1.52 (1.27, 1.81)** | **1.50 (1.26, 1.79)** | **1.39 (1.16, 1.67)** | **1.22 (1.01, 1.46)** | 1.06 (0.88, 1.28)    |
| WC       |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.06 (0.91, 1.30)    | 1.03 (0.85, 1.23)    | 1.03 (0.85, 1.23)    | 0.97 (0.80, 1.16)    | 0.89 (0.74, 1.07)    | 0.84 (0.70, 1.02)    |
| Q3       | **1.31 (1.11, 1.55)** | **1.28 (1.08, 1.52)** | **1.28 (1.07, 1.52)** | 1.17 (0.98, 1.40)    | 1.01 (0.84, 1.21)    | 0.93 (0.77, 1.11)    |
| Q4       | **1.78 (1.50, 2.11)** | **1.84 (1.54, 2.20)** | **1.83 (1.52, 2.19)** | **1.63 (1.36, 1.96)** | **1.34 (1.11, 1.62)** | 1.21 (1.00, 1.48)    |
| BMI      |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 0.99 (0.83, 1.18)    | 0.98 (0.82, 1.17)    | 0.98 (0.82, 1.17)    | 0.93 (0.77, 1.11)    | 0.81 (0.67, 0.97)    | 0.77 (0.64, 0.93)    |
| Q3       | 1.12 (0.95, 1.33)    | 1.17 (0.98, 1.39)    | 1.16 (0.97, 1.39)    | 1.07 (0.99, 1.28)    | 0.88 (0.73, 1.06)    | 0.82 (0.68, 0.98)    |
| Q4       | **1.51 (1.29, 1.78)** | **1.72 (1.45, 2.05)** | **1.71 (1.44, 2.03)** | **1.52 (1.28, 1.81)** | 1.17 (0.98, 1.41)    | 1.10 (0.91, 1.33)    |
| Triglyceride |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.04 (0.87, 1.25)    | 0.98 (0.82, 1.18)    | 0.99 (0.82, 1.19)    | 0.95 (0.79, 1.14)    | 0.90 (0.75, 1.09)    | 0.87 (0.72, 1.06)    |
| Q3       | **1.39 (1.17, 1.65)** | **1.33 (1.12, 1.59)** | **1.34 (1.12, 1.60)** | **1.23 (1.02, 1.47)** | 1.14 (0.95, 1.37)    | 1.07 (0.88, 1.29)    |
| Q4       | **1.58 (1.33, 1.86)** | **1.66 (1.40, 1.96)** | **1.66 (1.40, 1.98)** | **1.44 (1.20, 1.74)** | **1.29 (1.07, 1.57)** | **1.18 (0.97, 1.44)** |

Note: Model 1 was adjusted for age and center. Model 2 was additionally adjusted for occupation, current drinking habits, and CVD history. Model 3 was additionally adjusted for ALT, GGT, eGFR, and total cholesterol. Model 4 was additionally adjusted for SBP and DBP. Model 5 was additionally adjusted for HbA1c, FBG, and PBG.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; CVAI, Chinese Visceral Adiposity Index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; HbA1C, hemoglobin A1C; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; PBG, post-load blood glucose; SBP, systolic blood pressure; UACR, urinary albumin to creatinine ratio; WC, waist circumference; WHR, waist-to-hip ratio. The bold values represent p < 0.05.

*p < 0.05; **p < 0.01; ***p < 0.001.
TABLE 4  Association of CVAI, BMI, WC, WHR, and triglyceride with increased UACR in female participants.

| Variable | Module 0 OR (95% CI) | Module 1 OR (95% CI) | Module 2 OR (95% CI) | Module 3 OR (95% CI) | Module 4 OR (95% CI) | Module 5 OR (95% CI) |
|----------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| CVAI     |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.24 (1.11, 1.40)**  | 1.10 (0.98, 1.24)    | 1.11 (0.99, 1.26)    | 1.09 (0.97, 1.23)    | 0.98 (0.86, 1.11)    | 0.94 (0.83, 1.07)    |
| Q3       | 1.71 (1.53, 1.91)**  | 1.33 (1.18, 1.50)**  | 1.35 (1.19, 1.52)**  | 1.30 (1.15, 1.47)**  | 1.06 (0.94, 1.20)    | 0.98 (0.86, 1.11)    |
| Q4       | 2.76 (2.49, 3.07)**  | 1.90 (1.67, 2.16)**  | 1.89 (1.66, 2.15)**  | 1.79 (1.57, 2.04)**  | 1.33 (1.16, 1.53)**  | 1.16 (1.01, 1.34)*   |
| WHR      |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.14 (1.03, 1.27)**  | 1.06 (0.95, 1.18)    | 1.05 (0.94, 1.17)    | 1.04 (0.93, 1.16)    | 0.96 (0.86, 1.08)    | 0.92 (0.83, 1.03)    |
| Q3       | 1.24 (1.12, 1.37)**  | 1.19 (1.06, 1.33)*   | 1.17 (1.05, 1.31)*   | 1.15 (1.03, 1.28)*   | 1.02 (0.91, 1.14)    | 0.95 (0.84, 1.06)    |
| Q4       | 1.38 (1.25, 1.53)**  | 1.29 (1.14, 1.44)**  | 1.26 (1.12, 1.41)**  | 1.22 (1.06, 1.37)**  | 1.05 (0.93, 1.18)    | 0.94 (0.84, 1.07)    |
| WC       |                      |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.18 (1.06, 1.31)*   | 1.10 (0.98, 1.23)    | 1.10 (0.98, 1.22)    | 1.08 (0.97, 1.21)    | 0.97 (0.87, 1.09)    | 0.95 (0.85, 1.06)    |
| Q3       | 1.33 (1.20, 1.47)**  | 1.20 (1.08, 1.34)*   | 1.19 (1.06, 1.32)*   | 1.16 (1.04, 1.30)**  | 0.99 (0.89, 1.11)    | 0.95 (0.85, 1.06)    |
| Q4       | 1.65 (1.49, 1.83)**  | 1.58 (1.38, 1.73)**  | 1.52 (1.36, 1.70)**  | 1.47 (1.31, 1.64)**  | 1.17 (1.04, 1.32)    | 1.07 (0.95, 1.21)    |
| BMI      |                      |                      |                      |                      |                      |                      |
| Q1       | 1.06 (0.96, 1.18)    | 1.10 (0.99, 1.23)    | 1.10 (0.99, 1.23)    | 1.09 (0.97, 1.21)    | 0.99 (0.88, 1.10)    | 0.96 (0.86, 1.07)    |
| Q2       | 1.13 (1.02, 1.25)*   | 1.17 (1.05, 1.31)*   | 1.17 (1.05, 1.30)*   | 1.14 (1.02, 1.27)*   | 0.97 (0.86, 1.08)    | 0.92 (0.82, 1.02)    |
| Q3       | 1.37 (1.24, 1.51)**  | 1.51 (1.36, 1.68)**  | 1.49 (1.34, 1.66)**  | 1.44 (1.29, 1.60)**  | 1.14 (1.01, 1.27)*   | 1.05 (0.94, 1.18)    |
| Triglyceride |                   |                      |                      |                      |                      |                      |
| Q1       | 1                    | 1                    | 1                    | 1                    | 1                    | 1                    |
| Q2       | 1.29 (1.16, 1.44)**  | 1.08 (0.97, 1.22)    | 1.10 (0.98, 1.23)    | 1.10 (0.98, 1.24)    | 1.02 (0.91, 1.15)    | 1.00 (0.87, 1.12)    |
| Q3       | 1.60 (1.44, 1.74)**  | 1.19 (1.07, 1.34)*   | 1.21 (1.08, 1.35)*   | 1.21 (1.08, 1.36)**  | 1.09 (0.97, 1.23)    | 1.03 (0.91, 1.16)    |
| Q4       | 2.14 (1.93, 2.37)**  | 1.55 (1.40, 1.73)**  | 1.57 (1.41, 1.75)**  | 1.55 (1.38, 1.74)**  | 1.31 (1.16, 1.48)**  | 1.18 (1.04, 1.33)**  |

Note: Model 1 was adjusted for age and center. Model 2 was additionally adjusted for occupation, current drinking habits, and CVD history. Model 3 was additionally adjusted for ALT, GGT, eGFR, and total cholesterol. Model 4 was additionally adjusted for SBP and DBP. Model 5 was additionally adjusted for HbA1C, FBG, and PBG.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; CVAI, Chinese Visceral Adiposity Index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; HbA1C, hemoglobin A1C; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; PBG, post-load blood glucose; SBP, systolic blood pressure; UACR, urinary albumin to creatinine ratio; WC, waist circumference; WHR, waist-to-hip ratio. The bold values represent $p < 0.05$. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. 
| Variable | Normal blood pressure | Hypertension | Note |
|----------|----------------------|--------------|------|
|          | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Adjusted for age, center, occupation, current drinking habits, CVD history, ALT, GGT, eGFR, total cholesterol, HbA1c, FBG, and PBG. |
| Male     |     |     |     |     |     |     |     |     | Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CVAI, Chinese Visceral Adiposity Index; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; HbA1C, hemoglobin A1; PBG, post-load blood glucose; WC, waist circumference; WHR, waist-to-hip ratio. The bold values represents \( p < 0.05 \). |
| CVAI     | 1  | 0.77 (0.59, 1.02) | 0.76 (0.57, 1.02) | 1.00 (0.74, 1.35) | 1 | 1.03 (0.77, 1.38) | 1.09 (0.82, 1.44) | **1.54 (1.17, 2.01)** |
| BMI      | 1  | 0.77 (0.59, 0.99) | 0.73 (0.55, 0.98) | 0.90 (0.67, 1.22) | 1 | 0.87 (0.66, 1.14) | 0.96 (0.74, 1.25) | **1.33 (1.03, 1.72)** |
| WC       | 1  | 0.87 (0.67, 1.14) | 0.71 (0.53, 0.94) | 1.03 (0.76, 1.41) | 1 | 0.89 (0.67, 1.17) | 1.17 (0.91, 1.51) | **1.43 (1.10, 1.85)** |
| WHR      | 1  | 0.88 (0.67, 1.15) | 0.91 (0.68, 1.22) | 0.96 (0.71, 1.29) | 1 | 1.09 (0.84, 1.41) | 1.04 (0.81, 1.34) | 1.20 (0.94, 1.54) |
| Triglyceride | 1  | 0.83 (0.62, 1.11) | 0.94 (0.70, 1.26) | 0.99 (0.72, 1.36) | 1 | 0.92 (0.72, 1.19) | 1.14 (0.89, 1.45) | **1.30 (1.01, 1.67)** |
| Female   |     |     |     |     |     |     |     |     | * \( p < .05 \); ** \( p < .01 \); *** \( p < .001 \). |
| CVAI     | 1  | 0.96 (0.83, 1.11) | 0.92 (0.78, 1.08) | 1.12 (0.92, 1.35) | 1 | 1.00 (0.79, 1.27) | 1.17 (0.93, 1.47) | **1.41 (1.12, 1.78)** |
| BMI      | 1  | 0.99 (0.87, 1.15) | 0.91 (0.79, 1.06) | 1.11 (0.95, 1.30) | 1 | 1.01 (0.84, 1.21) | 1.02 (0.86, 1.21) | 1.15 (0.97, 1.36) |
| WC       | 1  | 0.97 (0.84, 1.11) | 0.94 (0.81, 1.09) | 1.03 (0.87, 1.22) | 1 | 1.02 (0.84, 1.23) | 1.09 (0.91, 1.31) | 1.25 (1.04, 1.49) |
| WHR      | 1  | 0.93 (0.81, 1.07) | 0.96 (0.83, 1.12) | 0.96 (0.81, 1.14) | 1 | 1.01 (0.84, 1.21) | 1.02 (0.85, 1.21) | 1.03 (0.86, 1.23) |
| Triglyceride | 1  | 0.98 (0.84, 1.14) | 0.94 (0.80, 1.11) | 1.12 (0.95, 1.33) | 1 | 1.07 (0.89, 1.29) | 1.18 (0.99, 1.42) | **1.32 (1.11, 1.58)** |
| Variable  | Normal blood glucose          | Diabetes or prediabetes |  
|-----------|-------------------------------|-------------------------|  
|           | Q1   | Q2   | Q3       | Q4       | Q1   | Q2   | Q3    | Q4    |
| Male      |      |      |          |          |      |      |      |      |
| CVAI      | 0.73 (0.51, 1.04)            | 0.87 (0.60, 1.26)       | 1.30 (0.89, 1.89) | 1      | 0.98 (0.77, 1.24) | 0.99 (0.79, 1.25) | **1.37 (1.10, 1.72)** |
| BMI       | 0.61 (0.44, 0.83)            | 0.82 (0.60, 1.11)       | 1.15 (0.84, 1.56) | 1      | 0.91 (0.72115)    | 0.88 (0.69, 1.11)  | **1.13 (0.90, 1.43)** |
| WC        | 0.66 (0.48, 0.91)            | 0.95 (0.70, 1.29)       | 1.32 (0.96, 1.82) | 1      | 1.03 (0.81, 1.31) | 1.02 (0.81, 1.28)  | **1.32 (1.04, 1.68)** |
| WHR       | 0.95 (0.70, 1.29)            | 0.87 (0.63, 1.20)       | 1.19 (0.86, 1.63) | 1      | 0.97 (0.77, 1.23) | 1.06 (0.84, 1.33)  | **1.19 (0.95, 1.49)** |
| Triglyceride | 0.84 (0.63, 1.15)    | 1.13 (0.83, 1.54)       | 1.10 (0.78, 1.55) | 1      | 0.91 (0.72, 1.17) | 1.10 (0.87, 1.40)  | 1.27 (0.99, 1.62)   |
| Female    |      |      |          |          |      |      |      |      |
| CVAI      | 0.85 (0.71, 1.02)            | 0.96 (0.79, 1.16)       | 1.08 (0.86, 1.39) | 1      | 1.07 (0.89, 1.28) | 1.09 (0.92, 1.30)  | **1.38 (1.15, 1.66)** |
| BMI       | 0.92 (0.79, 1.08)            | 0.87 (0.74, 1.02)       | 0.96 (0.81, 1.14) | 1      | 1.03 (0.88, 1.22) | 1.01 (0.86, 1.18)  | **1.18 (1.01, 1.38)** |
| WC        | 0.91 (0.77, 1.06)            | 0.87 (0.74, 1.03)       | 0.94 (0.78, 1.13) | 1      | 1.02 (0.86, 1.20) | 1.08 (0.92, 1.26)  | **1.27 (1.08, 1.50)** |
| WHR       | 0.96 (0.82, 1.15)            | 0.97 (0.83, 1.15)       | 0.84 (0.70, 1.02) | 1      | 0.95 (0.81, 1.11) | 1.01 (0.87, 1.18)  | 1.13 (0.96, 1.32)   |
| Triglyceride | 1.01 (0.86, 1.18)    | 1.08 (0.91, 1.27)       | **1.26 (1.05, 1.51)** | 1      | 0.96 (0.82, 1.14) | 0.97 (0.81, 1.15)  | 1.13 (0.95, 1.33)   |

*Note: Adjusted for age, center, occupation, current drinking habits, CVD history, ALT, GGT, eGFR, total cholesterol, SBP, and DBP.*

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CVAI, Chinese Visceral Adiposity Index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; SBP, systolic blood pressure; UACR, urinary albumin to creatinine ratio; WC, waist circumference; WHR, waist-to-hip ratio. The bold values represents p < 0.05.

*p < .05; **p < .01; ***p < .001.
abdominal visceral adiposity was more closely related to microalbuminuria than subcutaneous adipose tissue. Kim et al declared that the visceral adipose tissue cross-sectional area measured by CT was strongly connected with albuminuria among the healthy Asian populace. A 4-year prospective cohort investigation in Korea proved that research subjects with higher base line visceral adipose had several times the incremental danger of albuminuria. However, given the inconveniences of imaging techniques, a reliable obesity index is vital. The traditional obesity index, such as BMI could not distinguish whole-length adipose distribution, meanwhile, it might overpredict the hazard of illnesses among individuals with lots of muscle mass. WC and WHR are advantageous to use in clinical practice, but the correlation between WC or WHR and subcutaneous adiposity was stronger than that between WC or WHR and visceral adiposity. In addition, WC and WHR do not reflect the effect of height on disease risk. CVAI contains BMI, WC, age, and lipids, and CVAI is independent of somatotype.

Studies on the relationship between CVAI and UACR are scarce. Lu et al reported that CVAI had the strongest association with UACR among the abdominal obesity indices. The previous study concentrated on diabetics only, whereas the current study was large-scale, multicenter, and publicly engaged. The dependent variable UACR in their study was not classified according to clinical definitions, in the present study; however, UACR was classified according to clinical definitions. Besides, in our study, the relationship between increased UACR and CVAI was stratified based on blood pressure and blood glucose. The present study could be served as a supplement to the previous study, and the present study demonstrated that CVAI, as an obesity indicator that could predict albuminuria, was not only suitable for people with diabetes but also for the general population. This is important on account that clinically some people only have albuminuria without diabetes or kidney disease. The conclusions of the current study provide a way for the public that they could recognize albuminuria risk by elevated CVAI values and timely change abnormal adiposity distribution to postpone or refrain from the occurrence of albuminuria.

The relationship between CVAI and increased UACR has a slight gender difference. A study on 35 751 Chinese population found that triglyceride and UACR were significantly correlated only in women, whereas there was no correlation between triglyceride and UACR in men. A study of 35 848 Chinese population found that residues of triglyceride-rich lipoproteins were associated with UACR only in the female population but not in the male population. Hokanson conducted a meta-analysis based on the Framingham Heart Study, and he found that elevated triglyceride was more important for women than for men. In fact, although elevated triglyceride is proportional to the severity of albuminuria, when combined with overweight or obesity, the renal function is more likely to be damaged. We speculate that CVAI is highly associated with increased UACR because it is an indicator that includes both lipids and obesity measures. In the current study, although the OR value of CVAI was similar to that of triglyceride in the female population, the OR value of CVAI was higher than that of triglycerides in the male population, so we consider that CVAI could better predict UACR than triglyceride. Besides, previous studies have shown that women are more likely to have visceral obesity, and there is a greater association between visceral obesity and adverse metabolic outcomes in women, so we believe that women should be alert to the risk of albuminuria from visceral adiposity even if they are not overweight.

It is worth noting that after adjusting for SBP and DBP in model 4 and HbA1c, FBG, and PBG in model 5, the correlation between CVAI and UACR was attenuated, but still present. This indicates that abnormal metabolism might raise the risk of albuminuria. Many previous studies have shown important relationships between albuminuria, hyperglycemia, and hypertension, which could in part account for our findings. In the stratified analysis of the current study, we found that CVAI and UACR were significantly correlated in men and women with prediabetes, diabetes, and hypertension; thus we speculated that alterations in blood pressure and blood glucose were involved in the relationship between CVAI and albuminuria. Furthermore, some authors have suggested that excessive leptinemia and lipocalin deficiency in viscera obese patients may directly stimulate the renin-angiotensin-aldosterone system, which would lead to albuminuria and hypertension, and this could partly explain the stronger correlation between CVAI and UACR in the hypertensive population because hypertension and albuminuria might occur together in viscera obese patients. Besides, we found that in populations with hypertension or hyperglycemia, CVAI was better at discriminating elevated UACR than traditional obesity indices and triglycerides. Consequently, for individuals with abnormal blood pressure or blood glucose, reducing visceral adipose is equally critical as lowering blood pressure and glucose, and it is simple and feasible to monitor elevated CVAI to identify excess visceral adiposity and albuminuria risk.

The mechanism of the association between visceral adipose and albuminuria is worth discussing. (1) Adiponectin decreases as visceral fat increases, and previous
studies report an inverse association between adiponectin and proteinuria.\(^2\) (2) Leptin levels increase with increased visceral fat. Leptin causes albuminuria via inducing glomerular endothelial cell proliferation, increasing glomerular transforming growth factor-β1 (TGF-b1) expression, and increasing synthesis of type I collagen and type IV messenger RNA (mRNA).\(^3\) (3) The secretion of free fatty acids and interleukin 6 (IL-6) increases with the volume of visceral adipose tissue, which in turn contributes to macrophage infiltration and overproduction of tumor necrosis factor α (TNF-α), resulting in chronic inflammation and renal failure.\(^4\) (4) Superfluous visceral adipose compresses the kidneys and raises intrarenal pressure.\(^5\) (5) Superabundant visceral fat stimulates juxtaglomerular cells to secrete renin.\(^6\) (6) A slight increase in plasma aldosterone in visceral obese patients leads to salt and water retention, which in turn leads to albuminuria.\(^7\)

Thinking over the strong association between visceral adipose, albuminuria, and CVD, individuals with excess visceral fat ought to change their fat distribution rather than only weight loss. Regular exercise for 8 weeks to 1 year could reduce total, subcutaneous, and visceral adipose, and for exercise patterns, high-intensity interval training is more targeted to reduce visceral adipose than moderate intensity continuous training.\(^8\) Besides, a combination of a low-calorie diet and regular exercise is more effective in improving adipose distribution.\(^9\) Furthermore, when diet control and regular exercise are not effective, a combination of orlistat could also contribute to reducing excess visceral adipose tissue.\(^10\)

The first advantage of this study was the large sample size, and the inspection is very detailed, therefore, the confounders could be fully adjusted. Second, the samples were community based, so they could represent the general population of China. Third, the relationship between CVAI and increased UACR was investigated in a general Chinese population, for which no previous studies have been conducted. Nevertheless, there were some limitations. First, the current study was cross-sectional, thus, we could only draw conclusions about the association, not causation. Prospective cohort studies are needed in the future. Second, we did not measure UACR multiple times, but we limit urine collection to the first morning to minimize the impact of daytime activity.

5 CONCLUSION

Generally speaking, in the Chinese general population, CVAI was closely associated with increased UACR in both genders. Besides, at higher CVAI levels, the population with prediabetes, diabetes, or hypertension had a higher risk of albuminuria. We believe that CVAI could be a credible and convenient predictor of albuminuria and has guidance meaning to assist individuals to maintain healthy bodily form, especially for people with hyperglycemia or hypertension.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest in this work.

ETHICAL APPROVAL

The study protocol was approved by the Committee on Human Research at Rui-Jin Hospital affiliated with the School of Medicine, Shanghai Jiao Tong University. Written informed consents were obtained from all participants before data collection.

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