Urinary Albumin-Creatinine Ratio (UACR), Even within Normal Range, and Risk of Hypertension (HTN), Type 2 Diabetes Mellitus (T2DM), HTN with T2DM, Dyslipidemia and Cardiovascular Diseases in the Chinese Population: A Report from REACTION Study

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Research Article

Keywords:

Posted Date: January 28th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1292378/v1>

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Abstract

Background: Albuminuria has been widely considered as a risk factor for cardiovascular diseases (CVDs) which is associated with hypertension (HTN), type 2 diabetes mellitus (T2DM), HTN with T2DM and dyslipidemia. However, it is unclear the association between albuminuria and HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs. Thus, this study is aimed to thoroughly explore the association of albuminuria, even within the normal range, with the abovementioned diseases in the Chinese population.

Methods: This study included 40188 participants aged over 40 years from seven centers across China. Urinary albumin-creatinine ratio (UACR) was firstly divided into the ≥ 30 mg/g group, indicating kidney damage, and < 30 mg/g group. Furtherly, UACR was divided into five groups: the $< 20\%$ group, the 20–39% group, the 40–59% group, the 60–79% group and the $\geq 80\%$ group, according to quintile division of participants within the normal range. Propensity score matching was used to reduce bias, and multiple logistic regression models were conducted to examine the association between UACR and HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs.

Results: Multivariable regression analysis revealed that UACR, even within the normal range, is significantly associated with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs, and the association between UACR and HTN with T2DM was most significant in model 3 even after adjusting for confounding factors (HTN: OR: 1.76, 95%CI: 1.65-1.88, $P<0.0001$; T2DM: OR: 1.98, 95%CI: 1.84-2.12, $P<0.0001$; HTN with T2DM: OR: 2.37, 95%CI: 2.19-2.57, $P<0.0001$; Dyslipidemia: OR: 1.08, 95%CI: 1.01-1.14, $P=0.0154$; CVDs: OR: 1.14, 95%CI: 1.02-1.27, $P=0.0244$). In the stratified analysis, high normal UACR was significantly associated with HTN, T2DM, HTN with T2DM, dyslipidemia in subgroups.

Conclusions: We conclude the higher prevalence of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in abnormal UACR and reveal a significant association of UACR, even within the normal range, with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs.

Introductions

There is a growing population of elderly adults with hypertension (HTN), diabetes, dyslipidemia and cardiovascular diseases(CVDs) of increasingly complexity and a corresponding rise in health care burdens. Indicators that stratify risk for the general population across the metabolic abnormalities would possess great clinical value.

Albuminuria has been widely recommended as an indicator of renal damage. Emerging data has shown that albuminuria is not only an initial manifestation of renal function loss, but also a nonnegligible risk factor for CVDs especially in population with diabetes, HTN or dyslipidemia¹⁻³. Among diabetic adults in the United States, the prevalence of diabetic kidney disease (DKD) is about 34.5%, and 16.8% present with albuminuria⁴. Further, evidence is increasing that the presence of albuminuria indicates a 2.5-fold increased risk of stroke, which is consistent with the findings delivered by Norfolk's research^{5,6}. Moreover, albuminuria as measured by urine albumin to creatinine ratio (UACR), even within the normal range, is an effective predictor of HTN⁷. Similarly, a 5-year-follow-up study conducted in Korean men, demonstrated that high normal

albuminuria (UACR<30mg/g) could predict the increased risk of diabetes⁸. A robust body of literature has reported a strong, positive association between albuminuria and dyslipidemia in prediabetic and general population^{9,10}. Hence, albuminuria is valuable in identifying the general population at risk for CVDs, diabetes, HTN and dyslipidemia in clinical practice.

Previous studies have described an association between albuminuria and related metabolic diseases. However, little literature placed focus on the prevalence of diabetes, HTN, diabetes with HTN and dyslipidemia in the Chinese population with different UACR level. The present study is the first population-based study in the Chinese population and may uncover the incidence of diabetes, HTN, diabetes with HTN and dyslipidemia in individuals with different UACR level. Therefore, this current study is aimed to investigate the prevalence of diabetes, HTN, diabetes with HTN and dyslipidemia in different albuminuria range and explore the internal association between albuminuria and metabolic abnormalities.

Methods And Materials

Study population and design

The present study was drawn from the REACTION (Risk Evaluation of Cancers in Chinese Diabetic Individuals) study, which was conducted to investigate the association of diabetes and prediabetes with the risk of cancer in the Chinese population. Detailed information of the REACTION study has been described previously¹¹. The REACTION study was set up as a multi-center prospective observational study, and our study used baseline data from seven centers across China. A total of 47808 participants aged over 40 years were recruited from May and December 2012. (Liaoning 10140, Gansu 10026, Guangzhou 9743, Sichuan 8105, Shanghai 6821, Henan 1978, Hubei 995). Participants diagnosed with kidney diseases, cancer, fatty liver, viral hepatitis, cirrhosis, those using ACEI/ARB medicines and those with missing data were excluded. Then, 41757 participants were enrolled. Given differences in the baseline characteristics between the two different UACR groups, the propensity score matching was performed to reduce potential bias. Ultimately, 40188 eligible participants were included in this final analysis. (Figure 1).

The staff received extensive training related to the study questionnaire and outcome measures before the investigation. The study was conducted in accordance with Declaration of Helsinki, and the protocol was approved by the Clinical Research Ethics Committee of Rui-Jin Hospital affiliated with the School of Medicine, Shanghai Jiao Tong University. Written informed consents were obtained from all participants before the study.

Data collection and measurements

Data collection was performed by the well-trained staff, which included a standardized questionnaire, anthropometric measurements, blood collection, urine collection and a 75 g OGTT or 100 g steamed-bread meal test. The self-administered questionnaire consisted of demographic information, the history of diabetes, HTN, dyslipidemia, kidney diseases, hepatic diseases, CVDs (coronary heart disease (CHD),

myocardial infarction (MI), stroke), the current use of drugs, lifestyle including alcohol consumption and smoking consumption. Alcohol consumption was defined as follows: never; occasional drinkers who drank less than once a week; regular drinkers who drank at least once a week for over six months. Smoking consumption were defined as follows: never; occasional smokers who smoked less than one cigarette per day or less than 7 cigarettes per week; regular smokers who smoked at least one cigarette per day.

Anthropometric measurements, including the measurements of height, weight, waist circumference (WC) and blood pressure, were performed by the same well-trained staff. All participants were required to be in light clothing and take off shoes when weight and height were measured to the nearest 0.1 cm and 0.1 kg. WC was measured to the nearest 0.1 cm at the umbilical level when participants were in a standing position¹². Body mass index (BMI) was calculated using the following formula: $BMI = \text{body weight} / \text{height}^2$ (kg/m^2). Blood pressure and heart rate (HR) were recorded three times consecutively by the same well-trained staff at 5-min intervals after participants were in a seated position for at least 5 min at rest. The three measurements of blood pressure and HR were averaged for the final analysis.

Blood samples were collected by the experienced nurses in the morning after at least 12 h of overnight fasting. Participants with or without a history of diabetes underwent a 100 g steamed-bread meal test or 75 g OGTT, respectively. After 2 h, the second venous blood samples were obtained by the same well-trained nurses. Fasting plasma glucose (FPG), 2 h post-load blood glucose (PBG), Haemoglobin A1c (HbA1c), serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and creatinine (Cr) were measured at every center.

The estimated glomerular filtration rate (eGFR) was calculated on the basis of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)¹³.

Definition of Variables

Fasting midstream urine samples were collected in the morning to measure the concentration of urine albumin and urine creatinine by using chemiluminescence immunoassay in every center. UACR was calculated by dividing urine albumin in milligrams by urine creatinine in grams. The same range and units of UACR measurement were used in all seven centers. According to the KDIGO CKD guidelines, increased albuminuria was defined as $UACR \geq 30 \text{ mg/g}$, indicating kidney damage¹⁴.

According to the WHO guidelines, type 2 diabetes mellitus (T2DM) was defined as $FBG \geq 7.0 \text{ mmol/L}$, or $PBG \geq 11.1 \text{ mmol/L}$, or diagnosed as T2DM by clinicians and meanwhile undergoing hypoglycemic-medication therapy. HTN was defined as systolic blood pressure (SBP) $\geq 140 \text{ mmHg}$ or diastolic blood pressure (DBP) $\geq 90 \text{ mmHg}$, or diagnosed as HTN by clinicians and meanwhile undergoing antihypertensive-medication therapy. Dyslipidemia was defined as increased TC ($\geq 6.20 \text{ mmol/L}$), LDL-C ($> 4.13 \text{ mmol/L}$), TG ($> 2.25 \text{ mmol/L}$), decreased HDL-C ($< 1.03 \text{ mmol/L}$), or a combination of the above lipid abnormalities. HTN with T2DM was defined as a combination of HTN and T2DM. Stroke was defined as a self-reported history of language or physical dysfunction lasting over 24 h and ischemic or hemorrhagic

stroke by imageological diagnosis. CHD events were defined as a self-report history of myocardial infarction or angina, or coronary revascularization by clinicians. CVDs were defined as a self-reported history of CHD, stroke, or myocardial infarction events.

Participants were divided into three groups according to their smoking frequency: no: never or have already quit smoking; occasional: smoking less than once a week or less than 7 cigarettes weekly; frequently: smoking one or more cigarettes daily for at least a half year. Similarly, participants were divided into three groups according to their alcohol intake frequency: no: never or have already quit drinking; occasional: drinking less than once a week; frequently: drinking more than once a week for at least a half year.

Statistical analysis

Empower(R) (www.empowerstats.com, X&Y Solutions Inc., Boston, MA) and R (<http://www.Rproject.org>) were used to perform the statistical analyses. Given differences in the baseline characteristics between eligible participants between the two groups of UACRs, propensity score matching was employed to control for potential bias. Matching was performed using a 1:7 matching protocol to match all covariates, with a calliper width equal to 0.05 of the SD of the logit of the propensity score.

Continuous variables with a non-normal distribution were presented as median (Q1-Q3), and those with a normal distribution were presented as means $\pm$ the standard deviations (SD). Categorical variables were expressed as n%. Differences in continuous variables were compared using the Kruskal–Wallis test, and when variables were categorical, the χ^2 test was used. Multivariate logistic regression analysis was performed to control potential confounding factors for identifying the associations of UACR with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in three models. Model 1 was unadjusted. Model 2 was adjusted for age and BMI. Model 3 was further adjusted for sex; SBP; DBP; HR; ALT; AST; eGFR; smoking habits, drinking habits, FBG, PBG, TC, TG, HDL-C, LDL-C and history of medication. The odds ratio (OR) and corresponding 95% confidence intervals (95% CI) were calculated.

To thoroughly explore the associations between UACR and HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs, multivariate logistic regression analysis was also conducted in participants with normal albuminuria (UACR < 30 mg/g). Further, in order to examine the internal link of the relationship between UACR and HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs, subgroups were stratified by the different history of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in the stratified analyses. All statistical tests were two-sided, and P values < 0.05 were considered statistically significant.

Results

Clinical characteristics of the study population

After propensity score matching, a total of 40188 participants with a median age (Q1-Q3) of 57.58 (52.40-63.93) years were included in this study, including 12223 (30.41%) men and 27965 (69.59%) women (Table 1). Table 1 shows that 6205 (15.44%) of participants had T2DM, 17386 (43.26%) had HTN, 2225 (5.54%)

had CVDs, and 17071 (42.34%) had dyslipidemia. Compared to non-hypertensive participants, the hypertensive ones were older, had a larger BMI, ALT, AST, SBP, DBP, HR, TC, TG, LDL-C, FBG, PGB, HbA1c, UACR, lower eGFR, were less frequent smokers, more frequent drinkers, and a higher prevalence of T2DM, HTN with T2DM, CVDs and dyslipidemia (Table S1). Compared to non-T2DM participants, the diabetic ones were older, had a larger BMI, ALT, SBP, DBP, HR, TG, FBG, PGB, HbA1c, UACR, lower eGFR, LDL-C and HDL-C, were more frequent smokers and drinkers, and a higher prevalence of HTN, HTN with T2DM, CVDs and dyslipidemia. Similar results were found in HTN with T2DM. Similarly, participants with dyslipidemia had an inferior control of blood pressure, glucose, lipid, a higher prevalence of HTN, T2DM, CVDs, and were more frequent smokers, drinkers (Table S1-S4).

Associations of UACR with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in the total population

Multiple logistic regression models that consider the association of albuminuria with the individual prevalence of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs were constructed. Table 2 shows OR and 95% CI of HTN, T2DM, HTN with T2DM, dyslipidemia, CVDs with continuous UACR and categories of UACR in the total population of three different models. As seen in Table 2, UACR is significantly associated with HTN, T2DM, HTN with T2DM, dyslipidemia, CVDs in model 1-2. Even after further adjustments in model 3, UACR remained significantly associated with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs. However, in model 3, the adjusted OR of UACR (≥ 30 mg/g) was not as remarkable as it in model 2, but the association of UACR with HTN with T2DM was most significant in model 3 (HTN: OR: 1.89, 95%CI: 1.77-2.01, $P < 0.0001$ in model 3 VS OR: 1.76, 95%CI: 1.65-1.88, $P < 0.0001$ in model 3; T2DM: OR: 2.21, 95%CI: 2.06-2.36, $P < 0.0001$ in model 2 VS OR: 1.98, 95%CI: 1.84-2.12, $P < 0.0001$ in model 3; HTN with T2DM: OR: 2.50, 95%CI: 2.31-2.70, $P < 0.0001$ in model 2 VS OR: 2.37, 95%CI: 2.19-2.57, $P < 0.0001$ in model 3; Dyslipidemia: OR: 1.18, 95%CI: 1.12-1.25, $P < 0.0001$ in model 2 VS OR: 1.08, 95%CI: 1.01-1.14, $P = 0.0154$ in model 3; CVDs: OR: 1.30, 95%CI: 1.17-1.45, $P < 0.0001$ in model 2 VS OR: 1.14, 95%CI: 1.02-1.27, $P = 0.0244$ in model 3), indicating the blood glucose, pressure and lipid level possessing the effects of the metabolic diseases. The association between continuous values of UACR is also shown in Table 2, which was consistent with the findings delivered by categorical values.

Associations of UACR with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in participants with normal UACR (<30mg/g)

To thoroughly explore the association of albuminuria with such diseases, multiple logistic regression models were also constructed in participants with normal range of albuminuria (UACR < 30 mg/g) as shown in Table 3. These results indicate that compared with participants with lower UACR levels, participants with higher normal UACR levels (**HTN**: the second quintile to the fifth quintile; **T2DM**: the second quintile to the fifth quintile; **HTN with T2DM**: the second quintile to the fifth quintile; **Dyslipidemia**: the third quintile to fifth quintile; **CVDs**: the fifth quintile) were also significantly associated with HTN, T2DM, HTN with T2DM,

dyslipidemia and CVDs, even after adjustments for confounding factors in model 3. In model 3, the ORs for HTN were increased significantly from the second quintile, with ORs 1.08 (1.01, 1.16) for quintile 2, 1.29 (1.20, 1.39) for quintile 3, 1.45 (1.35, 1.56) for quintile 4, and 1.55 (1.40, 1.72) for quintile 5. Similar results and tendency were observed in T2DM, HTN with T2DM, dyslipidemia and CVDs (**T2DM**: Q2: OR 1.18, 95%CI 1.06-1.31, P=0.0025, Q3: OR 1.35, 95%CI 1.22-1.50, P<0.0001; Q4: OR 1.67, 95%CI 1.51-1.85, P<0.0001; Q5: OR 2.17, 95%CI 1.90-2.48, P<0.0001; **HTN with T2DM**: Q2: OR 1.29, 95%CI 1.13-1.49, P=0.0002, Q3: OR 1.45, 95%CI 1.26-1.65, P<0.0001; Q4: OR 1.90, 95%CI 1.67-2.17, P<0.0001; Q5: OR 2.32, 95%CI 1.96-2.75, P<0.0001; **Dyslipidemia**: Q3: OR 1.12, 95%CI 1.05-1.19, P=0.0009; Q4: OR 1.12, 95%CI 1.04-1.19, P=0.0011; Q5: OR 1.14, 95%CI 1.03-1.26, P=0.0090; **CVDs**: Q5: OR 1.23, 95%CI 1.00-1.51, P=0.0463). Similar positive associations were detected in participants with the normal range of albuminuria when UACR was a continuous variable (**HTN**: OR 1.02, 95%CI 1.02-1.03, P<0.0001; **T2DM**: OR 1.08, 95%CI 1.01-1.16, P=0.0286; **HTN with T2DM**: OR 1.04, 95%CI 1.03-1.04, P<0.0001; **Dyslipidemia**: OR 1.01, 95%CI 1.00-1.01, P=0.0005; **CVDs**: OR 1.01, 95%CI 1.00-1.01, P=0.0940).

Stratified analysis of associations between UACR and HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in participants with normal UACR (<30mg/g)

Stratified analyses were conducted in the different subgroups of HTN, T2DM, dyslipidemia and CVDs to validate the abovementioned results, shown in Table 4. The present study found that compared with lower UACR, higher normal UACR (the third, fourth and fifth quintiles) was closely associated with HTN in both subgroups of HTN, T2DM, dyslipidemia and CVDs. To be noted, these associations were most significant in participants that were both in the subgroup of the fifth quintile of UACR and the subgroups of normal blood glucose (OR 1.64, 95%CI 1.14-1.88, P<0.0001), dyslipidemia (OR 1.58, 95%CI 1.35-1.84, P<0.0001) and CVDs (OR 1.83, 95%CI 1.16-2.89, P=0.0097). Similarly, the most significant association of UACR with T2DM were both in the fifth quintile of UACR subgroup and normal blood pressure (OR 2.50, 95%CI 2.05-3.06, P<0.0001), normal blood lipid level (OR 2.15, 95%CI 1.77-2.61, P<0.0001) and CVDs-free (OR 2.20 95%CI 1.91-2.54, P<0.0001) subgroups. The association between the fifth quintile of UACR and HTN with T2DM was more significant in dyslipidemia (OR 2.54, 95%CI 2.02-3.18, P<0.0001) and CVDs-free (OR 2.37, 95%CI 1.98-2.83, P<0.0001) subgroups. The most significant association of the fifth quintile of UACR with dyslipidemia was detected in participants without HTN (OR 1.15 95%CI 1.01-1.32, P=0.0399) and without T2DM (OR 1.13 95%CI 1.02-1.27, P=0.0245). However, no significant association between the fifth quintile of UACR and CVDs was observed in subgroups of HTN, T2DM and dyslipidemia.

Discussion

Main findings

As far as we all know, this is the first study conducted in a Chinese general population to observe the prevalence of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs with different UACR level and explore the

associations between albuminuria and the above diseases, even when albuminuria within the normal range. The following are the main findings of this current study: (1) compared with participants with normal albuminuria (UACR < 30 mg/g), participants with abnormal albuminuria (UACR $\geq$ 30 mg/g) had a higher prevalence of HTN (40.26% VS 61.11%), T2DM (13.27% VS 28.34%), HTN with T2DM (7.79% VS 20.71%), dyslipidemia (41.48% VS 47.49%) and CVDs (4.98% VS 8.88%), indicating the close relationship between albuminuria and metabolic diseases. (2) UACR is significantly associated with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs after adjusting for a wide spectrum of confounding factors. (3) High normal UACR is also associated with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs, and the association between high normal UACR and HTN with T2DM is most significant. (4) Further stratification shows that when UACR is at a high normal level (in the fifth quintile), participants without diabetes, with dyslipidemia and CVDs, have higher risks of HTN; those without HTN, dyslipidemia, and CVDs, have higher risks of T2DM; those with dyslipidemia and without CVDs, have higher risks of HTN with T2DM; those without HTN, T2DM and with CVDs, have higher risks of dyslipidemia. Therefore, UACR is an effective discriminator for the risk of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs, even when it is within the normal range. It is not only people with abnormal UACR but that those with high normal UACR should be vigilant the detection, prevention, and control of blood glucose, pressure, lipids to prevent and decrease the incidence of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs.

UACR and HTN

It is widely accepted that HTN is an important risk factor contributing to mortality worldwide and albuminuria plays a crucial role in the initiation and progression of HTN in previous studies^{15,16}. This research has described that albuminuria excretion more than 6 mg per day can effectively predict the progression of HTN. Notably, a growing number of studies performed in western population have pointed out that a significant association between albuminuria and HTN was not restricted to abnormal albuminuria (UACR $\geq$ 30 mg/g); albuminuria below the normal threshold (UACR < 30 mg/g) was also found associated with HTN. The Framingham Heart Study has reported that men with UACR > 6.66 mg/g and women with > 15.24 mg/g had an approximately 2-fold risk of HTN, indicating UACR being a useful biomarker for identifying individuals at high risk for HTN¹⁷. Moreover, a positive association between UACR within the normal range and HTN was revealed in postmenopausal women without diabetes, suggesting the revaluation of normal albuminuria excretion¹⁸.

Similarly, we found that not only abnormal UACR, but also an increase in UACR even within the normal range is closely associated with HTN, especially in people with T2DM and CVDs. Although the prevalence of HTN was higher in people with abnormal UACR than those with normal UACR (61.11% VS 40.26%), people with high normal UACR (the fifth quintile) have a 1.55-fold risk of HTN than those with low UACR (the first quintile) within the normal range in our study (Table 4). Our results showed clearly that high normal UACR is closely associated with HTN and the association is independent of eGFR levels, which was consistent with previous studies. Systemic and glomerular vascular abnormalities were thought to be a physiologic link between albuminuria and HTN^{19,20}. The presence of albuminuria could be caused by physiologic abnormalities of glomerular endothelial cells, the glomerular basement membrane, or podocytes, leading to

increased filtration of albumin. It is likely that increased albuminuria reflects generalized microvascular endothelial cell damage²¹, which possibly predispose to an increased atherogenic lipoproteins accumulation within subendothelial cell space²². A cohort study based on Japanese population, which followed 412 normotensive individuals without diabetes for a median 6.7 years, observed that a slight increase in UACR was closely associated with the incidence of HTN and is a predictor of increased blood pressure and incident HTN²³, suggesting that increased UACR in this current study is partly due to increased blood pressure below the level of diagnosis of HTN.

UACR and T2DM

There is strong evidence that albuminuria could be well indicative of microvascular dysfunction²¹. Compared with individuals without T2DM, the microvascular function of individuals with T2DM is markedly impaired^{24,25}. Louis et al. pointed out that the levels of albuminuria were independently associated with the severity of cardiac macrovascular function in individuals with T2DM²⁶. Although among diabetic individuals with normal ventricular diastolic function, the prevalence of cardiac macrovascular dysfunction was higher, especially in those with abnormal albuminuria, which was in line with our results. UACR is significantly higher in individuals with T2DM than those without T2DM in the present research (Table 1), indicating a close link between UACR and T2DM. It was well proved that UACR is not only a known indicator of kidney damage but also an effective predictor of atherogenic state. Accordingly, the results of population-based studies supported that UACR is valuable in predicting cardiovascular outcomes in clinical practice^{27,28}.

Interestingly, we noted that albuminuria, even within the normal range, is closely associated with T2DM in our study. Participants with abnormal albuminuria ($\text{UACR} \geq 30 \text{ mg/g}$) had a 1.98-fold risk of T2DM than those with the normal range ($\text{UACR} < 30 \text{ mg/g}$) ($P < 0.0001$). When UACR within the normal range, participants with high normal albuminuria (the fifth quintile) were still more likely to have the incidence of T2DM (OR 2.17, 95%CI 1.90-2.48, $P < 0.0001$), and the association between high normal albuminuria and T2DM was more significant in participants without HTN and dyslipidemia. This difference may be explained, in part, by smaller sample size of HTN and dyslipidemia group than non-HTN and non-dyslipidemia group in our study. Further large sample and prospective studies are necessary to clarify the association between UACR and the incidence of T2DM in different levels of blood pressure and lipids.

UACR and CVDs

As we all know, albuminuria is an established risk factor for CVDs morbidity and mortality both in diabetic and hypertensive individuals. Moreover, in the national and international guidelines, albuminuria is recommended as a routine screening parameter in individuals at high risk for CVDs²⁹⁻³¹ and has been recognized as a significant indicator of the incidence of generalized atherosclerosis because of the close association of albuminuria with atherosclerotic risk factors and microvascular endothelial damage³². Findings from population-based studies have reported a significant relationship between albuminuria and CVDs^{27,28}. Studies on individuals without T2DM and HTN also reached similar conclusions, which was in

line with our findings.³³ A prospective study, including 2484 white subjects, found that non-diabetic individuals with albuminuria have a 1.38-fold increased risk of cardiovascular mortality after adjustment for a wide spectrum of risk factors and a markedly high 5.68-fold increased risk of cardiovascular mortality was observed in diabetic population³⁴. This significant association was also assessed in the general population in this research. Additionally, a study of 40548 individuals observed that a 2-fold increase in albuminuria conferred a 1.29-fold increase in the risk of cardiovascular mortality³⁵. The results of our study, which showed an association between abnormal UACR and CVDs in the general population in seven regions across China, agree with earlier ones. Participants with abnormal albuminuria (UACR ≥ 30 mg/g) had a 1.14-fold increased risk of CVDs than those with normal albuminuria in our study.

Interestingly, we noted that UACR, even within the normal range, exhibited a significant association with CVDs in our study even after adjusting for confounding factors. Several studies pointed out that low-grade albuminuria can predict the incidence of CVDs events and CVDs death³⁶. The Framingham Study, including middle-aged non-hypertensive and nondiabetic individuals with normal UACR, found that low-grade UACR well below the abnormal threshold can effectively indicate the development of CVDs³⁷. Any degree of albuminuria has been proven to be a risk factor for CVDs in diabetic and non-diabetic patients; the risk increases with albuminuria, even below the microalbuminuria cutoff³⁸. Every 3.5 mg/g increment in UACR conferred a 5.9% increased risk of CVDs across a wide spectrum of UACR after adjustment for age and sex³⁸. Arnlov J et al. proposed that a nearly 3-fold increased risk of CVDs in people without HTN and T2DM but with UACR ≥ 3.9 mg/g in men, ≥ 7.5 mg/g in women, which was equal to the sex-specific median value³⁷.

In our study, we also found a positive association between UACR within the normal range and the risk of CVDs. CVDs events have been pronounced to be predictable by UACR variation within the normal range³⁹. The discrepancies between UACR within the normal range and CVDs in different subgroups might account for the interaction of stratification variables with CVDs. It is documented that UACR was significantly associated with components of metabolic syndrome, including blood glucose, pressure and lipids level³⁶. ACC/AHA and ESC/EAS guidelines have recommended LDL-C to be the most crucial risk lipid factor and therapeutic goal for CVDs⁴⁰, and the association between UACR within the normal range and CVDs in participants with dyslipidemia was at the borderline significant level in our study. It is well noticing that despite the achievement of optimal LDL-C level, a worrisome number of CVDs events still occur in clinical practice^{41,42}. In fact, the contribution of other lipid components and subfractions to CVDs development is increasingly being recognized^{43,44}. Traditionally, high HDL-C was confirmed to be protective against the incidence and development of atherosclerosis, and low HDL-C was associated with increased risk of CVDs⁴⁵. However, recent clinical trials reported that low HDL-C is not a cause of atherosclerosis, as originally thought, renewed interest in elevated TG has been generated⁴⁶. A growing up of studies supported the theory that elevated TG has a remarkable association with increased risk of CVDs^{47,48}. Moreover, reports from the CACTI Study pointed out that TG independently predicted increased odds of both related CVDs and albuminuria in patients with diabetes. Apart from this, several studies placed great importance on the average levels and ideal targets of glycemic parameters, and it was shown that individuals with CVDs can benefit from well control of blood glucose^{49,50}. Although elevated glucose parameters have been treated as a modifiable

cardiovascular risk factor and a robust predictor of CVDs, HbA1c serves as a superior indicator of cardiovascular events than FBG and PBG in clinical practice⁵¹. This might account for the fluctuation of FBG and PBG in different individuals, which could be influenced by various factors. Lots of researches have been carried out on the relationship between HTN and CVDs. The relationship between blood pressure and the increased risk of CVDs has been reported to be graded and continuous, starting from 115/75 mmHg, well within what is thought to be the normotensive range⁵². In fact, it is of great importance to comprehensively consider the predicted risk of atherosclerotic CVDs rather than the level of blood pressure alone, as patients with high CVDs risk could derive the benefits from blood pressure lowering treatment⁵³. Moreover, an association has also been reported between albuminuria, stroke and peripheral vascular diseases in several studies^{6,54,55}. The presence of albuminuria may occur due to vascular damage, indicating systemic endothelial dysfunction. The abovementioned evidence may further support our findings. Thus, early identification and prevention of albuminuria is of great significance and could contribute to reducing the risk of CVDs.

Limitations

Our study was a multi-center study based on seven-region community population, which representatively demonstrate the distribution of different regions across China. However, there are still limitations in our study. First, the variables in our study were measured at the same time. As a feature of the cross-sectional study, only associations, rather than causality, can be determined. Thus, the association of UACR with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs should be further explored in follow-up studies. Second, because the elderly population were from China, the association among other ethnic populations are needed to be confirmed. Third, although the participants using ACEI/ARB were excluded in our study, the possibility that other medications may partially influence the association could not be eliminated. Herein, we emphasize the association between UACR, even within the normal range and increased risk of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs, and such people should be vigilant about the detection, avoidance and intervention of the presence of albuminuria.

Conclusion

In summary, we observe the higher prevalence of HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in abnormal UACR and reveal a significant association of UACR, even within the normal range, with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs. Thus, we propose that albuminuria might be a simple and efficient indicator of the metabolic diseases as well as CVDs and targeting the early prevention as well as intervention of albuminuria metabolism may increase the possibility of successful drug discovery in the field of CVDs and its related diseases.

Declarations

Availability of data and materials

The datasets used to support this study are not freely available due to participants' privacy protection.

Funding:

The study is supported by the Chinese Society of Endocrinology, the Key Laboratory for Endocrine and Metabolic Diseases of Ministry of Health (1994DP131044), the National Key New Drug Creation and Manufacturing Program of Ministry of Science and Technology (2012ZX09303006-001), the National High Technology Research and Development Program of China (863 Program, 2011AA020107), National Science Foundation of China (81300717), National Science and Technology Major Project 288 (2011ZX09307-001-08), the REACTION Study.

Acknowledgements:

We would like to thank the participants in this study.

Competing interests:

The authors declare no competing interests.

Consent for publication:

Not applicable.

Ethics approval and consent to participate:

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. Informed consents were provided by all participants before data collection.

Authors' contributions:

All authors have read and approved the final manuscript.

YM and JW contributed to the conception and design of the study. YL, KC, YW, WG, ZL, AW, WW, ZG, X T, LY, QW, ZL, GQ, LC, YH and LJ recruited the subjects and supervised the study. JW analyzed the data and wrote the initial draft of the paper. YM, JW, YL, YW, WG and ZL contributed to the writing, reviewing, and revising of the manuscript.

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Tables

Table 1 Characteristics of total population

Variables	All participants
Age	57.58 (52.40-63.93)
BMI	24.34 (22.19-26.64)
ALT	15.00 (11.00-21.00)
AST	20.00 (17.00-25.00)
SBP	130.00 (117.00-145.00)
DBP	77.00 (70.00-84.00)
HR	78.00 (71.00-86.00)
TC	5.06 (4.33-5.79)
TG	1.38 (0.98-1.99)
LDL-C	2.94 (2.36-3.55)
HDL-C	1.29 (1.09-1.52)
FBG	5.54 (5.11-6.19)
PBG	7.41 (6.02-9.78)
HbA1c	5.90 (5.60-6.30)
eGFR	95.32 (90.93-99.01)
UACR	10.17 (5.92-20.13)
Sex	N (%)
men	12223 (30.41%)
women	27965 (69.59%)
Smoking	
No	34287 (85.32%)
Occasional	1209 (3.01%)
Frequently	4692 (11.68%)
Drinking	
No	30136 (74.99%)
Occasional	7457 (18.56%)
Frequently	2595 (6.46%)
Antihypertensive drugs	
Yes	6452 (16.05%)

No	33736 (83.95%)
Hypoglycemic drugs	
Yes	3776 (9.40%)
No	36412 (90.60%)
T2DM	
Yes	6205 (15.44%)
No	33983 (84.56%)
HTN	
Yes	17386 (43.26%)
No	22802 (56.74%)
CVDs	
Yes	2225 (5.54%)
No	37963 (94.46%)
Dyslipidemia	
Yes	17017 (42.34%)
No	23171 (57.66%)

Data were mean $\pm$ SD or median (Q1-Q3) for non-normal distribution of variables or numbers (%) for categorical variables

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ALT: alanine transferase; AST: aspartate transferase; HR: hearts rate; TG: triglyceride; TC: high cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FBG: fasting plasma glucose; PBG: 2 h post-load blood glucose; HbA1c: glycosylated hemoglobin; eGFR: estimated glomerular filtration rate; T2DM: type 2 diabetes mellitus; CVDs: cardiovascular diseases; UACR: urinary albumin to creatinine ratio

Table 2 Associations of UACR with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in the general population.					
Exposure	Model 1		Model 2		Model 3
	OR 95%CI P-value		OR 95%CI P-value		OR 95%CI P-value
HTN					
Continuous UACR	1.00 (1.00, 1.00) <0.0001		1.00 (1.00, 1.00) 0.0001		1.00 (1.00, 1.00) 0.0004
Categorical UACR					
<30 mg/g	1.0		1.0		1.0
≥ 30 mg/g	2.33 (2.20, 2.47) <0.0001		1.89 (1.77, 2.01) <0.0001		1.76 (1.65, 1.88) <0.0001
T2DM					
Continuous UACR	1.00 (1.00, 1.00) 0.0017		1.00 (1.00, 1.00) 0.0018		1.00 (1.00, 1.00) 0.0106
Categorical UACR					
<30 mg/g	1.0		1.0		1.0
≥ 30 mg/g	2.58 (2.42, 2.76) <0.0001		2.21 (2.06, 2.36) <0.0001		1.98 (1.84, 2.12) <0.0001
HTN with T2DM					
Continuous UACR	1.00 (1.00, 1.00) 0.0002		1.00 (1.00, 1.00) 0.0001		1.00 (1.00, 1.00) <0.0001
Categorical UACR					
<30 mg/g	1.0		1.0		1.0
≥ 30 mg/g	3.09 (2.87, 3.33) <0.0001		2.50 (2.31, 2.70) <0.0001		2.37 (2.19, 2.57) <0.0001
Dyslipidemia					
Continuous UACR	1.00 (1.00, 1.00) 0.1352		1.00 (1.00, 1.00) 0.2151		1.00 (1.00, 1.00) 0.4618
Categorical UACR					
<30 mg/g	1.0		1.0		1.0
≥ 30 mg/g	1.28 (1.21, 1.35) <0.0001		1.18 (1.12, 1.25) <0.0001		1.08 (1.01, 1.14) 0.0154
CVDs					
Continuous UACR	1.00 (1.00, 1.00) 0.4427		1.00 (1.00, 1.00) 0.7463		1.00 (1.00, 1.00) 0.8571
Categorical UACR					
<30 mg/g	1.0		1.0		1.0
≥ 30 mg/g	1.86 (1.68, 2.06) <0.0001		1.30 (1.17, 1.45) <0.0001		1.14 (1.02, 1.27) 0.0244

Model 1: unadjusted;

Model 2: adjusted for age, BMI,

Model 3: additionally adjusted for sex, ALT, AST, eGFR,SBP, DBP, HR, TG,TC, LDL,HDL, FBG,PBG,smoking, drinking, based on Model 2;

Abbreviations: OR: odds ratio; CI: confidential interval; BMI: body mass index; ALT: alanine transferase; AST: aspartate transferase; eGFR: estimated glomerular filtration rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: hearts rate; TG: triglyceride; TC: high cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FBG: fasting plasma glucose; PBG: 2 h post-load blood glucose; T2DM:type 2 diabetes mellitus; CVDs: cardiovascular diseases; UACR: urinary albumin to creatinine ratio

Table 3 Associations of UACR with HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in participants with normal UACR (<30mg/g).

Exposure	Model 1 OR 95%CI P-value	Model 2 OR 95%CI P-value	Model 3 OR 95%CI P-value
HTN			
Continuous UACR	1.03(1.03, 1.03). <0.0001	1.02(1.02, 1.03). <0.0001	1.02(1.02,1.03). <0.0001
UACR quintiles			
Q1	1.0	1.0	1.0
Q2	1.11 (1.04, 1.19) 0.0012	1.08 (1.01, 1.16). 0.0218	1.08 (1.01, 1.16). 0.0286
Q3	1.34 (1.25, 1.43). <0.0001	1.28 (1.19, 1.37). <0.0001	1.29 (1.20, 1.39). <0.0001
Q4	1.65 (1.55, 1.76). <0.0001	1.44 (1.34, 1.54). <0.0001	1.45 (1.35, 1.56). <0.0001
Q5	1.80 (1.64, 1.98). <0.0001	1.53 (1.38, 1.70). <0.0001	1.55 (1.40, 1.72). <0.0001
T2DM			
Continuous UACR	1.04 (1.03, 1.04). <0.0001	1.03 (1.03, 1.04). <0.0001	1.03 (1.03, 1.04). <0.0001
UACR quintiles			
Q1	1.0	1.0	1.0
Q2	1.21 (1.09, 1.34) 0.0003	1.18 (1.07, 1.31). 0.0013	1.18 (1.06, 1.31). 0.0025
Q3	1.42 (1.29, 1.57). <0.0001	1.35 (1.23, 1.50). <0.0001	1.35 (1.22, 1.50). <0.0001
Q4	1.89 (1.72, 2.07). <0.0001	1.69 (1.53, 1.86). <0.0001	1.67 (1.51, 1.85). <0.0001
Q5	2.41 (2.13, 2.74). <0.0001	2.14 (1.88, 2.44). <0.0001	2.17 (1.90, 2.48). <0.0001
HTNwith T2DM			
Continuous UACR	1.04 (1.04, 1.05). <0.0001	1.04 (1.03, 1.04). <0.0001	1.04 (1.03, 1.04). <0.0001
UACR quintiles			
Q1	1.0	1.0	1.0
Q2	1.34 (1.17, 1.53). <0.0001	1.30 (1.14, 1.49). 0.0002	1.29 (1.13, 1.49). 0.0002
Q3	1.57 (1.38, 1.79). <0.0001	1.44 (1.26, 1.65). <0.0001	1.45 (1.26, 1.65). <0.0001

Q4	2.26 (2.00, 2.55). <0.0001	1.91 (1.69, 2.17). <0.0001	1.90 (1.67, 2.17). <0.0001
Q5	2.72 (2.32, 3.19). <0.0001	2.28 (1.93, 2.68). <0.0001	2.32 (1.96, 2.75). <0.0001
Dyslipidemia			
Continuous UACR	1.01 (1.01, 1.01) <0.0001	1.01 (1.00, 1.01). <0.0001	1.01 (1.00, 1.01). 0.0005
UACR quintiles			
Q1	1.0	1.0	1.0
Q2	1.02 (0.96, 1.09). 0.4546	1.03 (0.96, 1.09). 0.4324	1.02 (0.96, 1.09). 0.5575
Q3	1.13 (1.06, 1.20). 0.0001	1.13 (1.06, 1.20). 0.0002	1.12 (1.05, 1.19). 0.0009
Q4	1.17 (1.10, 1.25). <0.0001	1.14 (1.07, 1.21). <0.0001	1.12 (1.04, 1.19). 0.0011
Q5	1.21 (1.10, 1.33). <0.0001	1.17 (1.06, 1.28). 0.0017	1.14 (1.03, 1.26). 0.0090
CVDs			
Continuous UACR	1.02 (1.02, 1.03). <0.0001	1.01 (1.00, 1.02). 0.0063	1.01 (1.00, 1.01). 0.0940
UACR quintiles			
Q1	1.0	1.0	1.0
Q2	1.08 (0.92, 1.26). 0.3428	1.00 (0.86, 1.17). 0.9811	0.99 (0.85, 1.16). 0.9049
Q3	1.28 (1.11, 1.49). 0.0010	1.10 (0.95, 1.28). 0.2117	1.09 (0.94, 1.27). 0.2627
Q4	1.49 (1.29, 1.72). <0.0001	1.13 (0.97, 1.31). 0.1178	1.08 (0.93, 1.25). 0.3274
Q5	1.82 (1.50, 2.21). <0.0001	1.34 (1.10, 1.64). 0.0042	1.23 (1.00, 1.51). 0.0463

Model 1: unadjusted;

Model 2: adjusted for age, BMI,

Model 3: additionally adjusted for sex, ALT, AST, eGFR, SBP, DBP, HR, TG, TC, LDL, HDL, FBG, PBG, smoking, drinking, based on Model 2;

Abbreviations: OR: odds ratio; CI: confidential interval; BMI: body mass index; ALT: alanine transferase; AST: aspartate transferase; eGFR: estimated glomerular filtration rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: hearts rate; TG: triglyceride; TC: high cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FBG: fasting plasma glucose; PBG: 2 h post-load

blood glucose; T2DM:type 2 diabetes mellitus; CVDs: cardiovascular diseases; UACR: urinary albumin to creatinine ratio

Table 4 Stratified analysis of associations between UACR and HTN, T2DM, HTN with T2DM, dyslipidemia and CVDs in participants with normal UACR (<30mg/g) in model 3.

Exposure	HTN		T2DM		Dyslipidemia		CVDs	
	OR 95%CI P-value		OR 95%CI P-value		OR 95%CI P-value		OR 95%CI P-value	
	No	Yes	No	Yes	No	Yes	No	Yes
HTN								
Continuous UACR			1.02 (1.02, 1.03) <0.0001	1.02 (1.01, 1.03) 0.0001	1.02 (1.02, 1.03) <0.0001	1.02 (1.02, 1.03) <0.0001	1.02 (1.02, 1.03) <0.0001	1.03 (1.01, 1.05) 0.0002
UACR quintiles								
Q1			1.0	1.0	1.0	1.0	1.0	1.0
Q2			1.06 (0.98, 1.14) 0.1287	1.31 (1.07, 1.61) 0.0091	1.09 (0.99, 1.19) 0.0826	1.07 (0.96, 1.19) 0.2155	1.10 (1.02, 1.18) 0.0107	0.82 (0.59, 1.14) 0.2459
Q3			1.31 (1.22, 1.42) <0.0001	1.29 (1.06, 1.58) 0.0113	1.29 (1.18, 1.42) <0.0001	1.27 (1.15, 1.42) <0.0001	1.29 (1.20, 1.39) <0.0001	1.25 (0.90, 1.73) 0.1822
Q4			1.46 (1.35, 1.58) <0.0001	1.58 (1.30, 1.92) <0.0001	1.43 (1.30, 1.57) <0.0001	1.46 (1.32, 1.63) <0.0001	1.47 (1.36, 1.58) <0.0001	1.39 (1.00, 1.93) 0.0474
Q5			1.64 (1.46, 1.84) <0.0001	1.46 (1.14, 1.88) 0.0032	1.51 (1.31, 1.74) <0.0001	1.58 (1.35, 1.84) <0.0001	1.53 (1.38, 1.71) <0.0001	1.83 (1.16, 2.89) 0.0097
T2DM								
Continuous UACR	1.04 (1.03, 1.05) <0.0001	1.03 (1.02, 1.03) <0.0001			1.03 (1.02, 1.04) <0.0001	1.03 (1.03, 1.04) <0.0001	1.03 (1.03, 1.04) <0.0001	1.03 (1.02, 1.05) 0.0001
UACR quintiles								
Q1	1.0	1.0			1.0	1.0	1.0	1.0
Q2	1.12 (0.96, 1.30) 0.1446	1.25 (1.08, 1.45) 0.0028			1.30 (1.12, 1.51) 0.0004	1.05 (0.90, 1.22) 0.5222	1.17 (1.05, 1.30) 0.0049	1.27 (0.86, 1.88) 0.2201
Q3	1.43 (1.23, 1.66) <0.0001	1.34 (1.16, 1.54) <0.0001			1.35 (1.17, 1.57) <0.0001	1.33 (1.15, 1.53) <0.0001	1.36 (1.22, 1.51) <0.0001	1.33 (0.91, 1.93) 0.1373

Q4	1.74 (1.50, 2.02) <0.0001	1.68 (1.46, 1.92) <0.0001			1.68 (1.45, 1.95) <0.0001	1.62 (1.41, 1.86) <0.0001	1.65 (1.49, 1.83) <0.0001	1.98 (1.38, 2.84) 0.0002
Q5	2.50 (2.05, 3.06) <0.0001	2.02 (1.68, 2.42) <0.0001			2.15 (1.77, 2.61) <0.0001	2.11 (1.75, 2.55) <0.0001	2.20 (1.91, 2.54) <0.0001	1.86 (1.18, 2.95) 0.0081
HTN with T2DM								
Continuous UACR					1.03 (1.02, 1.04) <0.0001	1.04 (1.03, 1.05) <0.0001	1.04 (1.03, 1.04) <0.0001	1.03 (1.01, 1.05) 0.0002
UACR quintiles								
Q1					1.0	1.0	1.0	1.0
Q2					1.35 (1.10, 1.65) 0.0037	1.24 (1.02, 1.49) 0.0274	1.32 (1.14, 1.53) 0.0002	1.07 (0.70, 1.65) 0.7597
Q3					1.44 (1.17, 1.75) 0.0004	1.42 (1.18, 1.71) 0.0002	1.46 (1.27, 1.69) <0.0001	1.22 (0.81, 1.83) 0.3468
Q4					1.81 (1.49, 2.19) <0.0001	1.91 (1.61, 2.28) <0.0001	1.90 (1.66, 2.18) <0.0001	1.82 (1.24, 2.67) 0.0023
Q5					1.96 (1.52, 2.54) <0.0001	2.54 (2.02, 3.18) <0.0001	2.37 (1.98, 2.83) <0.0001	1.85 (1.13, 3.03) 0.0138
Dyslipidemia								
Continuous UACR	1.01 (1.00, 1.01) 0.0029	1.01 (1.00, 1.01) 0.0137	1.01 (1.00, 1.01) 0.0052	1.01 (1.00, 1.02) 0.0873			1.01 (1.00, 1.01) 0.0014	1.01 (1.00, 1.03) 0.0887
UACR quintiles								
Q1	1.0	1.0	1.0	1.0			1.0	1.0
Q2	1.06 (0.98, 1.15) 0.1506	0.97 (0.87, 1.08) 0.5983	1.05 (0.98, 1.12) 0.1864	0.80 (0.66, 0.97) 0.0260			1.02 (0.95, 1.09) 0.6392	1.11 (0.81, 1.52) 0.5134
Q3	1.17	1.07	1.12	1.03			1.10	1.41

	(1.08, 1.27) 0.0003	(0.96, 1.18) 0.2245	(1.05, 1.20) 0.0014	(0.85, 1.25) 0.7384		(1.03, 1.18) 0.0036	(1.04, 1.91) 0.0252
Q4	1.15 (1.05, 1.26) 0.0016	1.09 (0.99, 1.21) 0.0835	1.11 (1.04, 1.20) 0.0029	1.03 (0.86, 1.24) 0.7473		1.11 (1.04, 1.19) 0.0024	1.30 (0.96, 1.75) 0.0893
Q5	1.15 (1.01, 1.32) 0.0399	1.14 (0.99, 1.32) 0.0663	1.13 (1.02, 1.27) 0.0245	1.08 (0.85, 1.37) 0.5193		1.14 (1.03, 1.26) 0.0126	1.24 (0.83, 1.84) 0.2911
CVDs							
Continuous UACR	0.99 (0.98, 1.01) 0.3881	1.01 (1.00, 1.02) 0.0572	1.00 (1.00, 1.01) 0.3992	1.01 (0.99, 1.02) 0.2324	1.00 (0.99, 1.01) 0.8428	1.01 (1.00, 1.02) 0.0349	
UACR quintiles							
Q1	1.0	1.0	1.0	1.0	1.0	1.0	
Q2	1.17 (0.91, 1.50) 0.2137	0.88 (0.71, 1.08) 0.2078	0.96 (0.80, 1.15) 0.6418	1.07 (0.75, 1.52) 0.7076	0.92 (0.74, 1.14) 0.4346	1.08 (0.85, 1.36) 0.5444	
Q3	1.06 (0.82, 1.37) 0.6545	1.05 (0.86, 1.27) 0.6316	1.08 (0.91, 1.28) 0.4045	1.10 (0.78, 1.54) 0.5884	0.92 (0.74, 1.13) 0.4166	1.31 (1.05, 1.64) 0.0188	
Q4	0.95 (0.73, 1.23) 0.6832	1.07 (0.89, 1.29) 0.4910	0.97 (0.82, 1.16) 0.7709	1.30 (0.95, 1.78) 0.1038	0.94 (0.76, 1.15) 0.5439	1.25 (1.00, 1.55) 0.0526	
Q5	1.01 (0.69, 1.49) 0.9542	1.24 (0.97, 1.59) 0.0829	1.25 (0.99, 1.59) 0.0624	1.14 (0.76, 1.70) 0.5323	1.18 (0.89, 1.56) 0.2595	1.29 (0.96, 1.74) 0.0898	

Model 1: unadjusted;

Model 2: adjusted for age, BMI,

Model 3: additionally adjusted for sex, ALT, AST, eGFR, SBP, DBP, HR, TG, TC, LDL, HDL, FBG, PBG, smoking, drinking, based on Model 2;

Abbreviations: OR: odds ratio; CI: confidential interval; BMI: body mass index; ALT: alanine transferase; AST: aspartate transferase; eGFR: estimated glomerular filtration rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: hearts rate; TG: triglyceride; TC: high cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FBG: fasting plasma glucose; PBG: 2 h post-load

blood glucose; T2DM: type 2 diabetes mellitus; CVDs: cardiovascular diseases; UACR: urinary albumin to creatinine

Figures

Figure 1

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