

A High Body Roundness Index Is More Closely Associated With Urinary Albumin-creatinine Ratio Than Traditional Adiposity Indices in Chinese Population: a Cross-sectional Report From the Reaction Study

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Research Article

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Abstract

Objective:

Body roundness index (BRI) has been proposed to be a promising index of body fat distribution. The association between BRI and increased albuminuria is unclear. Therefore, the aim of this study is to examine the discriminative ability of BRI for increased albuminuria and compare the association of BRI and traditional adiposity indices (body mass index: BMI, waist circumference: WC, waist-to-hip ratio: WHR) with albuminuria.

Methods:

This cross-sectional study was nested in an ongoing REACTION study. A total of 43591 participants aged over 40 years were recruited across seven different regional provinces. Increased albuminuria was defined as urinary albumin to creatinine ratio (UACR) ≥ 30 mg/g. Multiple logistic regression analyses were performed to detect the association between BRI and UACR and compare the discriminative ability of traditional (BMI, WC, WHR) and new adiposity indices (waist-to-height ratio: WHtR, BRI) with UACR.

Results:

Participants with increased UACR exhibited increased age, blood pressure, blood glucose, poor control of lipid level, decreased estimated glomerular filtration rate (eGFR) and higher prevalence of diabetes, hypertension and cardiovascular events. Multiple logistic models showed that compared with traditional adiposity indices (BMI, WC, WHR), the BRI index remained significantly associated with UACR especially in women, indicating the strong discriminative power for increased albuminuria. Stratified analysis revealed that the strong positive association of the BRI index with increased albuminuria also occurred in people who were young, women, poor control of hypertension and blood glucose, and $eGFR \geq 90$ ml/min/1.73².

Conclusions:

The BRI index were closely associated with increased albuminuria in the Chinese population.

Introduction

Elevated urinary albumin to creatinine ratio (UACR) has been recommended as an indicator of chronic kidney disease (CKD),¹ and a key risk factor for many chronic diseases. Romero-Aroca et al. indicated that compared with the estimated glomerular filtration rate (eGFR), UACR shows a stronger association with diabetic retinopathy.² Moreover, UACR can not only be predictive of cardiovascular disease (CVD), but also has important value in evaluating the left ventricular dysfunction.³ A recent study has demonstrated that UACR is closely associated with preeclampsia and could be used as an early predictor of preeclampsia in the pre-gestational diabetic population.⁴ Furthermore, UACR has been confirmed

associated with vascular damage. Not only in diabetic population, but also in patients with acute lacunar infarction, increased UACR is a significant indicator for cerebral small vessel diseases.⁵

A growing body of evidence have reported that obesity is a key driver of CKD,^{6,7} and increased UACR as an early indicator of CKD could effectively reflect the injury of glomerular and tubular cell function. Recently, body mass index (BMI), an easily applicable measure of obesity, has been reported to be closely associated with CKD progression in hypertensive patients.⁸ Framingham study cohort has suggested that high BMI could be independently predicting of the renal dysfunction,⁹ and it is valuable in predicting the onset of albuminuria.¹⁰ However, several studies has demonstrated that it is the accumulation of visceral fat rather than subcutaneous fat that promotes the development of CKD.¹¹⁻¹³ Although BMI, waist circumference (WC) and waist-to-hip ratio (WHR) are commonly used adiposity indices with the advantages of convenience, they provided limited information on the body fat distribution and body shape.¹⁴⁻¹⁶ Thus, it is important to find a simple and effective screening tool for albuminuria to reduce the incidence of CKD.

In recent years, a new anthropometric index, body roundness index (BRI), have been proposed as an indicator of body fat distribution and body shape, because it has a strong and stable relationship with the abdominal adipose accumulation. BRI, a predictor of body fat and visceral adipose tissue volume, has been confirmed to have the potential to identify the status of diabetes.¹⁷⁻¹⁹ It is well known that diabetes is an additional cause of CKD and obesity is the main pathogenetic pathway linking diabetes and CKD. However, the relationship between fat distribution and albuminuria is still unknown.

To the best of our knowledge, there are limited studies involving the relationship between BRI and albuminuria and it is still unclear that whether traditional adiposity indices or newly developed adiposity indices are more valuable in estimating the renal dysfunction. Therefore, the aim of this study is to examine the association between BRI with UACR and compare the discriminative ability of the traditional and new anthropometric indices for UACR.

Materials And Methods

Study population and design

This cross-sectional study was nested in a longitudinal REACTION (Risk Evaluation of Cancers in Chinese diabetic Individuals) study, which was designed to investigate the association between T2DM and the risk of cancer among the Chinese population. Details of the REACTION study have been previously reported.^{20,21} The present study used baseline investigation data from seven centers across China. Initially, a total of 45130 participants aged over 40 years were recruited from May 2011 to December 2011. Participants diagnosed with kidney or other related diseases, those using ACEI/ARB medicines and those with missing data were excluded as shown in Figure 1. Finally, 43591 participants were enrolled in the present study.

Before carrying out the investigation, the staff received extensive training, including the standardized questionnaire and data collection. The protocol of present study was approved by the Committee on Human Research at Rui-Jin Hospital affiliated with the School of Medicine, Shanghai Jiao Tong University. This study adhered to the principles of the Declaration of Helsinki. Written informed consents were obtained from all participants before data collection.

Data collection

Data collection were performed by the same trained staff, according to standardized operational procedures. All the participants received the same comprehensive examinations including a standard questionnaire, anthropometric measurements, venous blood collection, and 75-g oral glucose tolerance test (OGTT) or bread meal test. The questionnaire included the history of diabetes, hypertension, acute/chronic nephritis, nephritic syndrome, kidney stones, CVD, diabetes, alcohol habits, and smoking habits. Regular smokers were defined as those who smoked at least one cigarette per day. Occasional smokers were participants who smoked less than one cigarette per day or less than 7 cigarettes per week. Regular drinkers were defined as participants who consumed alcohol at least once a week for over six months. Occasional drinkers were defined as participants who drank less than once a week.

Height, weight, WC and hip circumference (HC) were measured by the same well-trained staff after participants were required to wear light clothing and take off the shoes. Height and weight were clinically measured in light clothing, using the same device with the precision of 0.01 m and 0.1 kg, respectively. WC was measured by the same staff placing a tape horizontally between the inferior costal margin and the superior border of iliac crest at the end of expiration and that was measured to the nearest 0.01m. HC was recorded at the maximum circumference over the buttocks, to the nearest 0.01m.

After resting for five minutes, participants' blood pressure and pulse were measured three times with in one-minute intervals by the same staff. The average of blood pressure was calculated and used in the statistical analysis. The pulse rate was measured while the blood pressure was recorded. After 8-10 of fasting overnight, the first fasting blood samples of all the participants were obtained. Patients without a history of T2DM underwent a 75 g OGTT; they were required to drink 300 mL of a glucose solution containing 75 g of glucose within 5 minutes. After 2 hours, the second venous blood sampling was obtained by the same well-trained staff. Fasting blood glucose (FBG), 2 h post-load blood glucose (PBG), serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and serum creatinine (Cr), Haemoglobin A1c (HbA1c), alanine transferase (ALT), aspartate transferase (AST), and gamma-glutamyl transferase (GGT) were respectively measured in every center.

The variables were defined as follows: hypertension (any self-reported history of hypertension or systolic blood pressure $SBP \geq 140$ mmHg or diastolic blood pressure $DBP \geq 90$ mmHg), T2DM ($FBG \geq 7.0$ mmol/L or $PBG \geq 11.1$ mmol/L simultaneously or any self-reported history of diabetes), cardiovascular events (any self-reported history of coronary heart disease, stroke, and myocardial infarction). According to the WHO criteria, prediabetes was defined as follows: $6.1 \leq FBG < 7.0$ mmol/L or $2h PBG < 11.1$

mmol/L. Based on WHO criteria, prediabetes was further divided into 3 groups as follows: impaired fasting glucose (IFG): $6.1 \leq \text{FBG} < 7.0$ mmol/L and $\text{PBG} < 7.8$ mmol/L; impaired glucose tolerance (IGT): $\text{FBG} < 6.1$ mmol/L and $7.8 \leq \text{PBG} < 11.1$ mmol/L; and IFG+IGT: $6.1 \leq \text{FBG} < 7.0$ mmol/L and $7.8 \leq \text{PBG} < 11.1$ mmol/L. eGFR was calculated based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).²²

Definition of UACR group and anthropometric indices

The concentration of urine albumin and creatinine were measured by collecting the first urine specimens in the morning. The definition of UACR was calculated using the following formula: urinary albumin (mg)/urinary creatinine (g). All seven centers used the same normal value range and unit of measurement as the following, normo-albuminuria: <30 mg/g; increased albuminuria ≥ 30 mg/g.

BMI was calculated using the formula: $\text{BMI} = \text{weight kg} / \text{height m}^2$. WHtR was calculated as the WC divided by the height. ABSI and BRI were calculated using the following formula: $\text{BRI} = 364.2 - 365.5 \times (1 - [\text{WC}/2\pi]^2 / [0.5 \times \text{height}^2])^{1/2}$. The BRI score was converted to a z-score using the following formula: $\text{BRI} - \text{BRI}_{\text{mean}} / \text{BRI}_{\text{SD}}$. BMI, WC, WHR, WHtR were also transformed to z-score by the same equation. Given difference of the unit change in the logistic regression analysis, the z-score were conducted to made the comparison meaningful.²³

Statistical analysis

The statistical analyses were performed using Empower(R) (www.empowerstats.com, X&Y Solutions Inc., Boston, MA) and R (<http://www.Rproject.org>). A p value < 0.05 (2-sided) was considered statistically significant.

Data were presented as median (25th percentile-75th percentile) for continuous variables of non-normal distribution. Category variables were presented as percentage (%). Differences in the continuous variables among the two subgroups of UACR were analyzed using the Kruskal-Wallis test. The category variables were tested using the chi-square test. Multiple logistic regression analysis was conducted to detect the association of traditional and new adiposity indices with UACR. The conventional risk variables related to renal dysfunction were adjusted,^{24,25} and confounding factors that when added to the model, changed the matched odds ratio (OR) by at least 10% were also selected for adjustment. Model I was adjusted for age and sex. To further correct the effects of the confounding factors, model II was adjusted for centers, age, sex, BMI, SBP, DBP, FBG, PBG, HbA1c, HDL, LDL, TG, GGT, eGFR, pulse, centers, smoking status, drinking status, and medication history. In order to thoroughly investigate the association and compare the difference in different levels of age, sex, eGFR, the control of blood pressure and glucose, stratified analyses were performed based on the subgroups of age (Age < 55 years, 55-64 years, ≥ 65 years), sex (men, women), the subgroup of eGFR ($\text{eGFR} \geq 90$ mL/min per 1.73 m^2 , $\text{eGFR} < 90$ mL/min per 1.73 m^2), blood glucose (normal: $\text{FBG} < 7.0$ mmol/L and/or $\text{PBG} < 11.1$ mmol/L, prediabetes : IFG: $6.1 \leq \text{FBG} < 7.0$ mmol/L and $\text{PBG} < 7.8$ mmol/L, IGT: $\text{FBG} < 6.1$ mmol/L and $7.8 \leq \text{PBG} < 11.1$ mmol/L, IFG + IGT: $6.1 \leq$

FBG < 7.0 mmol/L and $7.8 \leq$ PBG < 11.1 mmol/L, diabetes: FBG \geq 7.0 mmol/L and PBG \geq 11.1 mmol/L or any self-reported history of diabetes), blood pressure (normal blood pressure SBP <140 mmHg and diastolic blood pressure DBP < 90 mmHg, hypertension SBP \geq 140 mmHg or DBP \geq 90 mmHg or any self-reported history of hypertension).

Results

Demographic Data and Hematologic Parameters of the study population

A total of 43591 participants with a median age (Q1-Q3) of 57.51 (52.19-63.90) years were included in this study, including 13119 (30.10%) men and 30472 (69.90%) women as shown in Table 1. Table 1 shows the basic characteristics based on UACR range (UACR <30 or \geq 30 mg/g). Participants with increased UACR had increased age, SBP, DBP, pulse, FBG, PBG, HbA1c, AST, GGT, TG, eGFR, BMI Z score, WC Z score, WHtR Z score, WHR Z score, BRI Z score, as well as decreased TG, LDL, HDL, eGFR. Participants with the increased age have the higher risk of increased UACR. The prevalence of T2DM, hypertension, and CVD events were respectively higher in participants with increased UACR (T2DM: 28.05 % VS 13.11%, Hypertension: 60.04 % VS 28.05%, CVD events: 8.82 % VS 4.88%, $P < 0.001$).

Associations between adiposity indices and the risk of increased UACR in total population

Table 2 shows the significant association between all adiposity indices and UACR in the total population in Model I. After further adjusting for confounding factors in model II, the association between newly developed adiposity indices (WHtR and BRI) remained significant, indicating the stability of the association between WHtR, BRI and increased UACR (WHtR: OR: 1.08, 95% CI 1.02-1.13 $P = 0.0075$; BRI: OR: 1.22, 95% CI 1.11-1.33 $P = 0.0001$). However, the significant association between BMI, WHR, WC and increased UACR vanished, suggesting the inferior discriminative ability for albuminuria.

Associations between adiposity indices and increased UACR in stratified analyses

To verify the discriminative power of all adiposity indices for albuminuria, stratified analyses were performed in subgroups as shown in Table 3. In younger participants (age < 65 years), BRI was positively associated with the increased UACR, whereas other indices did not present a significant association with increased UACR in Model II (BRI: age < 55 years: OR: 1.41, 95% CI 1.20-1.66 $P = 0.0001$; $55 \leq$ age < 64 years: OR: 1.41, 95% CI 1.03-1.38 $P = 0.0203$). In women, only WHtR and BRI showed a significant association with increased UACR and the discriminative ability of BRI for UACR was superior to WHtR (BRI: OR: 1.29, 95% CI 1.16-1.43 $P < 0.0001$ VS WHtR: OR: 1.08, 95% CI 1.02-1.15 $P = 0.0083$). However, no significant association between BRI and UACR was found in men. Of note is the gender effect of BRI on UACR risk. In stratified analysis, a significant association between BRI and UACR was also observed in both hypertension and diabetes subgroups, but the association was more superior in those without hypertension and those with diabetes (Hypertension Yes: OR: 1.14 95% CI 1.01-1.28 $P = 0.0341$ VS Hypertension No: OR: 1.29 95% CI 1.12-1.48 $P = 0.0004$; Diabetes Yes: OR: 1.33 95% CI 1.13-1.57 $P = 0.0007$ VS Diabetes No: OR: 1.17 95% CI 1.07-1.28 $P = 0.0009$), indicating the additional risk of blood glucose on

increased albuminuria. To further explore the association of the effect of blood glucose on UACR, the participants with prediabetes were divided into IFG, IGT, and IFG+IGT. Table 4 shows that only BRI had a significant association with increased UACR in the IGT and IGT+IFG groups (IGT: FBG < 6.1 mmol/L and $7.8 \leq \text{PBG} < 11.1$ mmol/L: OR: 1.20, 95% CI 1.08-1.33, $P=0.0005$; IGT+IFG: $6.1 \leq \text{FBG} < 7.0$ mmol/L and $7.8 \leq \text{PBG} < 11.1$ mmol/L: OR:1.34, 95% CI 1.03-1.74, $P=0.0320$), suggesting the additional risk of poor control of 2h post-load blood glucose on increased UACR. Moreover, to thoroughly verify the association of BRI with UACR, stratified analysis was also conducted based on different renal functions, and we found similar results at different level of eGFR. When participants had a normal $\text{eGFR} \geq 90$ mL/min per 1.73 m^2 , the odds of having an increased UACR positively in participants with increased BRI (BRI: OR:1.26, 95% CI 1.13-1.41, $P<0.0001$). However, no significant association was found in participant with $\text{eGFR} < 90$ mL/min per 1.73 m^2 . The above results show that compared with traditional adiposity indices (BMI, WC, WHR), the new adiposity index BRI presented a superior discriminative ability for albuminuria, suggesting the advantage of BRI as an easy and effective screening tool for early kidney failure.

Discussion

Main findings

In the present study, we found that BRI was positively associated with UACR and showed a superior discriminative ability for UACR than traditional adiposity indices (BMI, WHR and WC), suggesting its advantage of being an accurate discriminator for the risk of albuminuria to early predict renal lesion. Stratified analysis revealed that participants with higher BRI were more likely to have albuminuria than those with lower BRI, especially in participants who were young (age <60 years), those with abnormal blood glucose ($\text{FBG} \geq 7.0$ mmol/L and $\text{PBG} \geq 11.1$ mmol/L), and those with normal blood pressure ($\text{SBP} \geq 140$ mmHg or diastolic blood pressure $\text{DBP} \geq 90$ mmHg) and eGFR ($\text{eGFR} \geq 90$ mL/min per 1.73 m^2). To the best of our knowledge, this is the first multicenter, large sample investigation to explore the association between BRI and UACR in the Chinese elderly population. Therefore, effective prevention and intervention are important for UACR, and modification of the body fat distribution and body shape may contribute to effectively reduce the incidence of adverse events in participants with poor control of blood glucose and blood pressure.

It is well known that obesity is a leading cause of chronic diseases, including CVD, T2DM, hypertension and CKD. Considering the use of computed tomography (CT) and magnetic resonance imaging (MRI) to detect body composition is accurate but expensive and inconvenient, previous studies proposed to use anthropometric indices to investigate the association between obesity and the risk of chronic diseases. Traditionally, BMI is a commonly recommended anthropometric index of the body fat. BMI has been reported to be valuable in predicting increased UACR.⁹ As well, it is closely associated with CKD among hypertensive patients as a predictor of the onset of albuminuria. Conversely,^{8,10} other studies opposed that BMI only indicates general obesity with less accuracy but not abdominal body fat, which plays a more significant role in the progression of chronic diseases.²⁶ Emerging evidence supported that it is abdominal obesity rather than general obesity that has superior predictive value for CVD risk.²⁷ Although

BMI has been the most commonly used adiposity index, it has limited power to distinguish peripheral from central body fat, fat and lean mass.^{28,29} Therefore, WC and WHR have been proposed as surrogate indices for abdominal obesity. Previous studies found that both WC and WHR are better predictors of CVD risk than BMI.³⁰⁻³² A recent study found WC to be more strongly associated with cardiometabolic risks than BMI, while another meta-analysis of 32 studies suggested WC, WHR and BMI have similar associations with the incidence of T2DM.^{33,34} In this present study, no significant difference was observed among WC, WHR, and BMI, which is consistent with previous studies. The results might be partially explained by the following reasons. First, WC and WHR have the insufficient capability of distinguishing visceral fat from subcutaneous fat, resulting in overestimating the visceral fat tissue in subjects. Second, WC and WHR may underestimate or overestimate the visceral fat without the consideration of height, which is an indicator of nutritional status during childhood.

In recent years, WHtR was also found to be a better screening tool for cardiometabolic risk factors than BMI and WC in a meta-analysis.³² A cross-sectional study revealed that WHtR was closely associated with cardiometabolic risk factors.³⁵ Moreover, another case-control study based on Chinese population found that WHtR showed the superior value in the assessment of CKD than BMI and WC, which is in line with our findings.³⁴

BRI, a novel and promising obesity-related index, combines height and WC and has been used to quantify the body shape and predict visceral fat tissue volume.²⁰ BRI has been proven to be more valuable in indicating body fat and visceral fat tissue than BMI and WC.²⁰ Some studies investigated that BRI is a better predictor of hyperuricemia than BMI in women. It is a superior index to investigate the association between obesity and hyperuricemia than WC and WHtR. Similarly, another cross-sectional study demonstrated that BRI presents a high predictive value to detect dyslipidemia in women.^{36,37} However, there is limited evidence on the comparison of the discriminative ability of BRI with other adiposity indices in identifying the risk of UACR. This present study was the first to access the superior ability of BRI to identify the risk of increased UACR compared with the traditional adiposity indices, indicating the advantage of BRI as an accurate and stable indicator of albuminuria.

Though the mechanism underlying the relationship between obesity and albuminuria is complex and unclear, it may be partially explained by the following reasons. It is well established that obesity can result in hemodynamic, hormonal and metabolic changes. First, obesity can induce increased renal plasma flow, glomerular pressure and filtration fraction, resulting in an increase in albuminuria.^{38,39} Second, it is reported that obesity activates the sympathetic nervous system and renin–angiotensin system (RAS) and physical compression of the kidneys, resulting in the increase of renal tubular sodium reabsorption and volume expansion, especially in the presence of visceral obesity. In addition, obesity can cause renal vasodilation and glomerular hyperfiltration. The results of these changes further lead to glomerular injury and urinary protein excretion.⁴⁰ Third, the relationship between visceral obesity and albuminuria may be linked to insulin resistance (IR). Accumulating evidence suggested that a characteristic feature of visceral obesity is increased free fatty acid (FFA) levels, which may contribute to the peripheral IR and dyslipidemia.⁴¹ The podocyte insulin signaling plays an important role of the

maintenance of the integrity of the glomerular filtration barrier. IR and lipo-toxicity induce the podocyte dysfunction, disrupting the integrity of the glomerular filtration barrier. This may be the initial step of diabetic nephropathy and the presence of albuminuria.⁴²⁻⁴⁴ The above-mentioned reasons might be possibly explained why the discriminative ability of BRI for the risk of UACR is superior to other adiposity indices.

In the clinical practice, it is convenient and highly cost-effective to use obesity-related indices to evaluate the visceral obesity and UACR risk. BRI showed the superior potential to be an accurate and stable indicator in the assessment of UACR. Hence, more attention should be paid to people with a high BRI to improve the distribution and deposition of visceral adiposity instead of only losing weight, in order to reduce CVD risk in clinical practice. We believe that taking BRI as part of management strategy is beneficial for reducing the diabetic nephropathy.

Limitations

Though the current study conducted in an aggregation of multi-community and the sample of our study was large, not only involved in 7 regions, but representing the general population in China. Several limitations, however, should be noted. Firstly, due to the design of this cross-sectional study, we can just investigate the association of different anthropometric indices with UACR and compared this relationship between new and traditional adiposity not cause. Second, though we excluded participants with related renal dysfunction and ACEI/ ARB medications, we did not detect other medications, possibly affecting the relationship. Furthermore, considering the convenience and price of measurements, we did not detect the distribution of body fat and abdominal fat percentage. Therefore, the conclusions should be draw with caution and more perfective studies should be needed to clarify the mechanisms underlying the relationship between anthropometric indices, especially BRI, and albuminuria.

Conclusions

In conclusion, this current study found that newly developed visceral adiposity index BRI was more closely associated with UACR compared with traditional adiposity indices (BMI, WHR, WC) and showed a superior discriminative ability for UACR in the general Chinese population. Considering that BRI is an accurate indicator of visceral body fat and body shape, people with borderline blood glucose, normal blood pressure and eGFR should pay more attention to control body shape and visceral body fat to reduce the risk of albuminuria and slow CKD progression rather than just weight loss for a low BMI. It is significant to identify people at high risk of albuminuria to take effective measures to decrease the incidence of CKD in the early status.

Declarations

Availability of data and materials

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

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Authors' contributions:

Jie Wang and Yun Wang have contributed equally to this work and share first authorship. Yiming Mu, Jie Wang and Yun Wang contributed to the conception and design of the study. Kang Chen, Binqi Li, Weiqing Wang, Zhengnan Gao, Xulei Tang, Li Yan, Qin Wan, Zuojie Luo, Guijun Qin and Lulu Chen recruited the subjects and supervised the study. Jie Wang, Yun Wang and Yang Liu analyzed the data and wrote the initial draft of the paper. Yiming Mu, Jie Wang and Yun Wang contributed to the writing, reviewing, and revising of the manuscript.

References

1. Levey AS, Becker C, Inker LA. Glomerular filtration rate and albuminuria for detection and staging of acute and chronic kidney disease in adults: a systematic review. *Jama* (2015) 313:837-46.
2. Romero-Aroca P, Baget-Bernaldiz M, Navarro-Gil R, et al. Glomerular Filtration Rate and/or Ratio of Urine Albumin to Creatinine as Markers for Diabetic Retinopathy: A Ten-Year Follow-Up Study. *J Diabetes Res* (2018) 2018:5637130.
3. Shogade TT, Essien IO, Ekrikpo UE, et al. Association of microalbuminuria with left ventricular dysfunction in Nigerian normotensive type 2 diabetes patients. *Cardiovasc J Afr* (2018) 29:283-8.
4. Zen M, Padmanabhan S, Cheung NW, et al. Microalbuminuria as an early predictor of preeclampsia in the pre-gestational diabetic population: A prospective cohort study. *Pregnancy Hypertens* (2019) 15:182-8.
5. Zhai Z, Feng J. Early microalbuminuria as a clinical marker for acute cerebral small vessel infarction. *Neurol Res* (2019) 41:151-5.
6. Zoccali C, Torino C, Tripepi G, Mallamaci F. Assessment of obesity in chronic kidney disease: what is the best measure? *Curr Opin Nephrol Hypertens* (2012) 21:641-6.

7. Adams KF, Schatzkin A, Harris TB, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med* (2006) 355:763-78.
8. Xie L, Wang B, Jiang C, et al. BMI is associated with the development of chronic kidney diseases in hypertensive patients with normal renal function. *J Hypertens* (2018) 36:2085-91.
9. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D. Predictors of new-onset kidney disease in a community-based population. *Jama* (2004) 291:844-50.
10. Garofalo C, Borrelli S, Minutolo R, Chiodini P, De Nicola L, Conte G. A systematic review and meta-analysis suggests obesity predicts onset of chronic kidney disease in the general population. *Kidney Int* (2017) 91:1224-35.
11. Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet* (2005) 366:1640-9.
12. Britton KA, Massaro JM, Murabito JM, Kreger BE, Hoffmann U, Fox CS. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. *J Am Coll Cardiol* (2013) 62:921-5.
13. Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. *Circulation* (2007) 116:39-48.
14. Field AE, Coakley EH, Must A, et al. Impact of overweight on the risk of developing common chronic diseases during a 10-year period. *Arch Intern Med* (2001) 161:1581-6.
15. Janssen I, Katzmarzyk PT, Ross R. Body mass index is inversely related to mortality in older people after adjustment for waist circumference. *J Am Geriatr Soc* (2005) 53:2112-8.
16. Ross R, Berentzen T, Bradshaw AJ, et al. Does the relationship between waist circumference, morbidity and mortality depend on measurement protocol for waist circumference? *Obes Rev* (2008) 9:312-25.
17. Krakauer NY, Krakauer JC. Dynamic association of mortality hazard with body shape. *PLoS One* (2014) 9:e88793.
18. Ji M, Zhang S, An R. Effectiveness of A Body Shape Index (ABSI) in predicting chronic diseases and mortality: a systematic review and meta-analysis. *Obes Rev* (2018) 19:737-59.
19. Chang Y, Guo X, Chen Y, et al. A body shape index and body roundness index: two new body indices to identify diabetes mellitus among rural populations in northeast China. *BMC Public Health* (2015) 15:794.
20. Thomas DM, Bredlau C, Bosy-Westphal A, et al. Relationships between body roundness with body fat and visceral adipose tissue emerging from a new geometrical model. *Obesity (Silver Spring)* (2013) 21:2264-71.
21. Maessen MF, Eijsvogels TM, Verheggen RJ, Hopman MT, Verbeek AL, de Vegt F. Entering a new era of body indices: the feasibility of a body shape index and body roundness index to identify cardiovascular health status. *PLoS One* (2014) 9:e107212.

22. Ning G. Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal (REACTION) study. *J Diabetes* (2012) 4:172-3.
23. Liu B, Liu B, Wu G, Yin F. Relationship between body-roundness index and metabolic syndrome in type 2 diabetes. *Diabetes Metab Syndr Obes* (2019) 12:931-5.
24. Lin CC, Li Cl, Liu CS, et al. Risks of decreased renal function and increased albuminuria for glycemic status and metabolic syndrome components: Taichung Community Health study. *Biomed Res Int* (2014) 2014:841497.
25. Eckardt KU, Coresh J, Devuyst O, et al. Evolving importance of kidney disease: from subspecialty to global health burden. *Lancet* (2013) 382:158-69.
26. Bergman RN, Stefanovski D, Buchanan TA, et al. A better index of body adiposity. *Obesity (Silver Spring)* (2011)19:1083-9.
27. Gwynn RC, Berger M, Garg RK, Waddell EN, Philburn R, Thorpe LE. Measures of adiposity and cardiovascular disease risk factors, New York City Health and Nutrition Examination Survey, 2004. *Prev Chronic Dis* (2011) 8:A56.
28. Gómez-Ambrosi J, Silva C, Galofré JC, et al. Body mass index classification misses subjects with increased cardiometabolic risk factors related to elevated adiposity. *Int J Obes (Lond)* (2012) 36:286-94.
29. Phillips CM, Tierney AC, Perez-Martinez P, et al. Obesity and body fat classification in the metabolic syndrome: impact on cardiometabolic risk metabotype. *Obesity (Silver Spring)* (2013) 21:E154-61.
30. Bibiloni Mdel M, Pons A, Tur JA. Defining body fatness in adolescents: a proposal of the AFAD-A classification. *PLoS One* (2013) 8:e55849.
31. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev* (2012) 13:275-86.
32. Savva SC, Tornaritis M, Savva ME, et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. *Int J Obes Relat Metab Disord* (2000) 24:1453-8.
33. Saqlain M, Akhtar Z, Karamat R, et al. Body Mass Index versus Other Adiposity Traits: Best Predictor of Cardiometabolic Risk. *Iran J Public Health* (2019) 48:2224-31.
34. Vazquez G, Duval S, Jacobs DR, Jr., Silventoinen K. Comparison of body mass index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta-analysis. *Epidemiol Rev* (2007) 29:115-28.
35. Janakiraman B, Abebe SM, Chala MB, Demissie SF. Epidemiology of General, Central Obesity and Associated Cardio-Metabolic Risks Among University Employees, Ethiopia: A Cross-Sectional Study. *Diabetes Metab Syndr Obes* (2020) 13:343-53.
36. Zhang N, Chang Y, Guo X, Chen Y, Ye N, Sun Y. A Body Shape Index and Body Roundness Index: Two new body indices for detecting association between obesity and hyperuricemia in rural area of China. *Eur J Intern Med* (2016) 29:32-6.

37. Zhang K, Zhao Q, Li Y, et al. Feasibility of anthropometric indices to identify dyslipidemia among adults in Jilin Province: a cross-sectional study. *Lipids Health Dis* (2018) 17:16.
38. Chagnac A, Weinstein T, Korzets A, Ramadan E, Hirsch J, Gafer U. Glomerular hemodynamics in severe obesity. *Am J Physiol Renal Physiol* (2000) 278:F817-22.
39. Henegar JR, Bigler SA, Henegar LK, Tyagi SC, Hall JE. Functional and structural changes in the kidney in the early stages of obesity. *J Am Soc Nephrol* (2001) 12:1211-7.
40. Hall JE, Henegar JR, Dwyer TM, et al. Is obesity a major cause of chronic kidney disease? *Adv Ren Replace Ther* (2004) 11:41-54.
41. Sarafidis PA, Bakris GL. Non-esterified fatty acids and blood pressure elevation: a mechanism for hypertension in subjects with obesity/insulin resistance? *J Hum Hypertens* (2007) 21:12-9.
42. Kim JA, Montagnani M, Koh KK, Quon MJ. Reciprocal relationships between insulin resistance and endothelial dysfunction: molecular and pathophysiological mechanisms. *Circulation* (2006) 113:1888-904.
43. Bornfeldt KE, Tabas I. Insulin resistance, hyperglycemia, and atherosclerosis. *Cell Metab* (2011) 14:575-85.
44. Jauregui A, Mintz DH, Mundel P, Fornoni A. Role of altered insulin signaling pathways in the pathogenesis of podocyte malfunction and microalbuminuria. *Curr Opin Nephrol Hypertens* (2009) 18:539-45.

Tables

Table 1: Characteristics of the participants in different groups of UACR

Variable	Total	UACR<30mg/g	UACR≥30mg/g	P-value
N	43591	37392	6199	
Age, years	57.51 (52.19-63.90)	57.03 (51.87-63.01)	61.04 (54.46-69.13)	<0.001
SBP, mmHg	131.00 (118.00-147.00)	130.00 (117.00-145.00)	141.00 (124.00-158.00)	<0.001
DBP, mmHg	77.00 (70.00-85.00)	77.00 (70.00-85.00)	79.00 (72.00-88.00)	<0.001
Pulse	79.00 (72.00-87.00)	78.00 (72.00-86.00)	80.00 (72.00-88.00)	<0.001
FBG, mmol/L	5.53 (5.11- 6.18)	5.50 (5.10-6.10)	5.80 (5.21-6.90)	<0.001
PBG, mmol/L	7.46 (6.08- 9.80)	7.31 (6.00- 9.47)	8.56 (6.61-12.30)	<0.001
HbA1c, %	5.90 (5.60- 6.30)	5.90 (5.60-6.20)	6.10 (5.70-6.70)	<0.001
ALT, U/L	15.00 (11.00-21.00)	15.00 (11.00-21.00)	15.00 (11.00-22.00)	<0.001
AST, U/L	20.00 (17.00-24.00)	20.00 (17.00-24.00)	21.00 (17.00-26.00)	<0.001
GGT, U/L	20.00 (15.00-31.00)	20.00 (14.00-31.00)	22.00 (15.00-35.00)	<0.001
TG, mmol/L	1.35 (0.96- 1.95)	1.32 (0.95-1.91)	1.55 (1.09-2.24)	<0.001
TC, mmol/L	5.02 (4.28- 5.76)	5.03 (4.29-5.77)	4.95 (4.21-5.71)	<0.001
LDL, mmol/L	2.91 (2.33- 3.53)	2.92 (2.34-3.54)	2.82 (2.23-3.43)	<0.001
HDL, mmol/L	1.28 (1.08- 1.51)	1.29 (1.09-1.52)	1.23 (1.04-1.45)	<0.001
eGFR, ml/min per 1.73 m ²	95.37 (90.96-99.12)	95.67 (91.45-99.41)	93.11 (87.87-97.63)	<0.001
Sex, %				<0.001
Male	13119 (30.10%)	11483 (30.71%)	1636 (26.39%)	
Female	30472 (69.90%)	25909 (69.29%)	4563 (73.61%)	
Drinking status, %				<0.001
No	32666 (74.94%)	27706 (74.10%)	4960 (80.01%)	
Occasional drinkers	8161 (18.72%)	7253 (19.40%)	908 (14.65%)	

Regular drinkers	2764 (6.34%)	2433 (6.51%)	331 (5.34%)	
Smoking				<0.001
No	37222 (85.39%)	31804 (85.06%)	5418 (87.40%)	
Occasional smokers	1357 (3.11%)	1198 (3.20%)	159 (2.56%)	
Regular smokers	5012 (11.50%)	4390 (11.74%)	622 (10.03%)	
Cardiovascular events	2371 (5.44%)	1824 (4.88%)	547 (8.82%)	<0.001
Hypertension	18293 (41.97%)	14571 (38.97%)	3722 (60.04%)	<0.001
Type 2 Diabetes mellitus	6642 (15.24%)	4903 (13.11%)	1739 (28.05%)	<0.001
Anthropometric indices				
BMI, kg/m ²	24.25 (22.08-26.57)	24.19 (22.04-26.47)	24.71 (22.46-27.17)	<0.001
BMI Z score	-0.06 (-0.65-0.57)	-0.08 (-0.66-0.54)	0.06 (-0.55-0.73)	<0.001
WC, cm	85.50 (79.00-93.00)	85.00 (79.00-92.00)	88.00 (80.50-95.00)	<0.001
WC Z score	0.01 (-0.64-0.75)	-0.04 (-0.64-0.65)	0.25 (-0.49-0.95)	<0.001
WHR	0.89 (0.84-0.93)	0.89 (0.84-0.93)	0.89 (0.85-0.94)	<0.001
WHR, Z score	0.01 (-0.61-0.61)	-0.01 (-0.62-0.59)	0.12 (-0.49-0.73)	<0.001
WHtR	0.53 (0.49-0.58)	0.53 (0.49-0.57)	0.55 (0.51-0.59)	<0.001
WHtR Z score	-0.01 (-0.65-0.66)	-0.05 (-0.67-0.60)	0.23 (-0.45-0.93)	<0.001
BRI	3.93 (3.16-4.82)	3.88 (3.14-4.75)	4.25 (3.39-5.21)	<0.001
BRI Z score	-0.07 (-0.66-0.60)	-0.11 (-0.67-0.54)	0.17 (-0.48-0.89)	<0.001

Data of characteristics expressed as median (25th percentile-75th percentile) for continuous variables of non-normal distribution and percentage (%) for categorical variables. SBP: systolic blood pressure; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; TG: triglyceride; TC: total cholesterol; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transpeptidase; FBG: 0-hour

fasting blood glucose; PBG: 2-hour postprandial blood glucose; HbA1c: haemoglobin A1c; BMI: body mass index; WC: waist circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio; ABSI: a body shape index; BRI: body roundness index.

Table 2: Associations between obesity indicators and UACR in total population

Variable	Non-adjusted	Model I	Model II
OR (95% CI) P-value		OR (95% CI) P-value	OR (95% CI) P-value
traditional indices of adiposity		1.12 (1.09, 1.15) <0.0001	1.00 (0.97, 1.04) 0.9093
BMI Z score	1.14 (1.11, 1.17) <0.0001		
WHR Z score	1.15 (1.12, 1.18) <0.0001	1.07 (1.04, 1.10) <0.0001	1.00 (0.96, 1.04) 0.9689
WC Z score	1.24 (1.20, 1.27) <0.0001	1.17 (1.14, 1.20) <0.0001	1.03 (0.98, 1.08) 0.2827
newly developed indices of adiposity		1.16 (1.13, 1.19) <0.0001	1.08 (1.02, 1.13) 0.0075
WHtR Z score	1.30 (1.27, 1.34) <0.0001		
BRI Z score	1.29 (1.25, 1.32) <0.0001	1.15 (1.12, 1.18) <0.0001	1.22 (1.11, 1.33) <0.0001

Non-adjusted model for none.

Model I adjusted for age and sex.

Model II adjusted for age, sex, BMI, center, SBP, DBP, pulse, LDL, HDL, TG, FBG, PBG, HbA1c, ALT, AST, GGT, eGFR, BMI Z score, WHR Z score, ABSI Z score, BRI Z score, smoking status, drinking status, history of hypertension, cardiovascular history, diabetes history, medication history.

Table 3: Associations between anthropometric indices and UACR in different subgroups

Subgroups	BMI Z score	WHR Z score	WC Z score	WHtR Z score	BRI Z score
	OR (95%CI) P-value	OR (95CI) P- value	OR (95% CI) P-value	OR (95% CI) P-value	OR (95% CI) P-value
Age					
Age < 55 years	1.01 (0.95, 1.08) 0.7443	1.04 (0.97, 1.12) 0.2809	0.99 (0.90, 1.10) 0.9051	1.08 (0.98, 1.20) 0.1370	1.41 (1.20, 1.66) <0.0001
55≥age<64years	0.99 (0.93, 1.05) 0.7063	0.97 (0.90, 1.04) 0.3372	1.01 (0.93, 1.10) 0.7461	1.05 (0.96, 1.14) 0.2800	1.19 (1.03, 1.38) 0.0203
Age ≥ 65 years	1.00 (0.94, 1.07) 0.8948	1.00 (0.93, 1.08) 0.9444	1.08 (0.98, 1.18) 0.1198	1.10 (1.00, 1.20) 0.0491	1.11 (0.95, 1.29) 0.2096
Sex					
men	1.01 (0.93,1.09) 0.8322	1.01 (0.92, 1.10) 0.8486	1.09 (0.98, 1.22) 0.1160	1.13 (1.00, 1.28) 0.0495	1.16 (0.95, 1.40) 0.1411
women	1.01 (0.97, 1.05) 0.7829	1.01 (0.96, 1.05) 0.7883	1.03 (0.97, 1.09) 0.3963	1.08 (1.02, 1.15) 0.0083	1.29 (1.16, 1.43) <0.0001
Hypertension					
Yes	1.07 (1.02, 1.12) 0.0075	1.00 (0.95, 1.06) 0.9490	1.05 (0.98, 1.13) 0.1518	1.09 (1.01, 1.17) 0.0242	1.14 (1.01, 1.28) 0.0341
No	0.95 (0.89, 1.00) 0.0645	1.01 (0.95, 1.07) 0.7085	1.01 (0.94, 1.10) 0.7341	1.07 (0.99, 1.16) 0.0790	1.29 (1.12, 1.48) 0.0004
Diabetes					
Yes	1.05 (0.99, 1.12) 0.1061	1.06 (0.98, 1.14) 0.1524	1.11 (1.01, 1.23) 0.0313	1.20 (1.09, 1.33) 0.0004	1.33 (1.13, 1.57) 0.0007
No	1.03	1.01	1.05	1.09	1.17

(1.00, 1.07) 0.0823 (0.97, 1.06) 0.5021 (1.00, 1.11) 0.0508 (1.03, 1.15) 0.0023 (1.07, 1.28) 0.0009

Model II adjusted for age, sex, BMI, center, SBP, DBP, pulse, LDL, HDL, TG, FBG, PBG, HbA1c, ALT, AST, GGT, eGFR, BMI Z score, WHR Z score, ABSI Z score, BRI Z score, smoking status, drinking status, history of hypertension, cardiovascular history, diabetes history, medication history.

Table 4: Associations between anthropometric indices and UACR in IFG, IGT, IFG+IGT

Subgroups	IFG		IGT		IFG+IGT	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
traditional anthropometric indices			0.99 (0.95, 1.03)	0.6455	1.10 (1.00, 1.21)	0.0595
BMI Z score	1.04 (0.89, 1.20)	0.6419				
WHR Z score	1.00 (0.82, 1.22)	0.9873	1.00 (0.96, 1.05)	0.8413	0.97 (0.87, 1.08)	0.5799
WC Z score	1.24 (0.97, 1.58)	0.0801	1.02 (0.96, 1.08)	0.5168	1.02 (0.89, 1.17)	0.8046
newly developed anthropometric indices			1.06 (1.00, 1.12)	0.0669	1.08 (0.94, 1.24)	0.2676
WHtR Z score	1.19 (0.91, 1.55)	0.2116				
BRI Z score	0.84 (0.53, 1.34)	0.4717	1.20 (1.08, 1.33)	0.0005	1.34 (1.03, 1.74)	0.0320

Model II adjusted for age, sex, BMI, center, SBP, DBP, pulse, LDL, HDL, TG, FBG, PBG, HbA1c, ALT, AST, GGT, eGFR, BMI Z score, WHR Z score, ABSI Z score, BRI Z score, smoking status, drinking status, history of hypertension, cardiovascular history, diabetes history, medication history.

Table 5: Associations between anthropometric indices and UACR in different subgroups of eGFR

Subgroups	eGFR < 90		eGFR ≥ 90	
	OR (95% CI)	P-value	OR (95% CI)	P-value
traditional anthropometric indices			1.01 (0.97, 1.06)	0.5514
BMI Z score	0.98 (0.91, 1.05)	0.5201		
WHR Z score	1.01 (0.94, 1.09)	0.7590	0.99 (0.95, 1.04)	0.7812
WC Z score	1.09 (0.99, 1.20)	0.0768	1.01 (0.95, 1.07)	0.8554
newly developed anthropometric indices			1.06 (0.99, 1.13)	0.0980
WHtR Z score	1.12 (1.01, 1.23)	0.0235		
BRI Z score	1.12 (0.95, 1.31)	0.1708	1.26 (1.13, 1.41)	<0.0001

Model II adjusted for age, sex, BMI, center, SBP, DBP, pulse, LDL, HDL, TG, FBG, PBG, HbA1c, ALT, AST, GGT, eGFR, BMI Z score, WHR Z score, ABSI Z score, BRI Z score, smoking status, drinking status, history of hypertension, cardiovascular history, diabetes history, medication history.

Figures

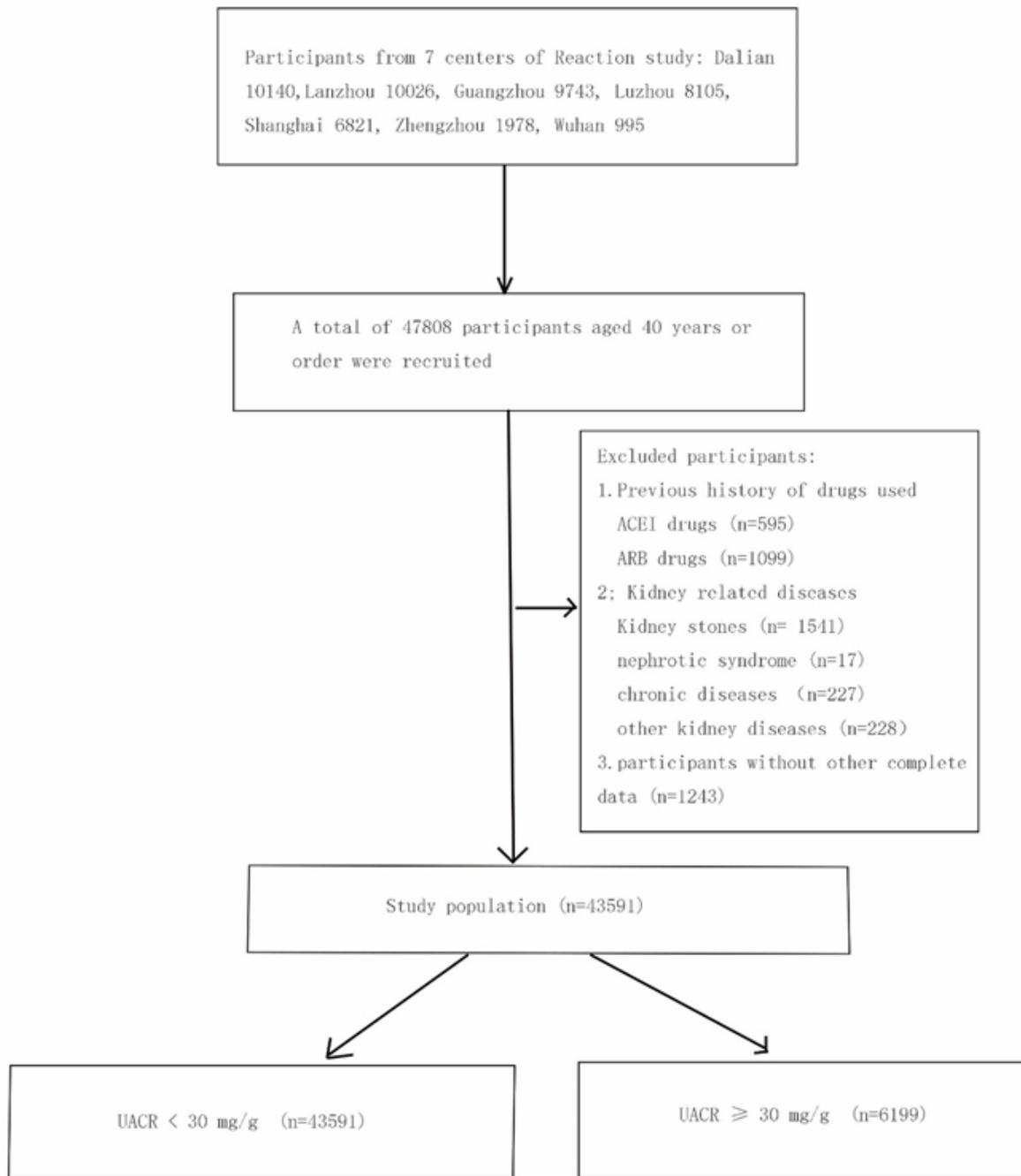


Figure 1

Flow chart of the selection of study participants