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# Association between obesity and urinary albumin-creatinine ratio in the middle-aged and elderly population of Southern and Northern China: a cross-sectional study

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## ABSTRACT

**Objective** The relationship between obesity and albuminuria has not been clarified. This study aimed to investigate the correlation between obesity and the urinary albumin-creatinine ratio (UACR) in Southern and Northern China.

**Design** A descriptive, cross-sectional study.

**Setting** Eight regional centres in REACTION (China's Risk Evaluation of cAncers in Chinese diabeTic Individuals, a lONgitudinal study), including Dalian, Lanzhou, Zhengzhou, Guangzhou, Guangxi, Luzhou, Shanghai and Wuhan.

**Participants** A total of 41 085 patients who were not diagnosed with chronic kidney disease (CKD) and had good compliance were selected according to the inclusion criteria. Patients who were diagnosed with CKD, who had other kidney diseases that could lead to increased urinary protein excretion, who were using angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers and whose important data were missing were excluded.

**Results** Participants with both, central and peripheral obesity, had a higher risk of elevated UACR, even after adjusting for multiple factors (OR: 1.14, 95% CI: 1.07 to 1.12, p<0.001), and the risk of high UACR in the South was more prominent than that in the North (OR $_{South}$: 1.22, 95% CI: 1.11 to 1.34; OR $_{North}$: 1.13, 95% CI: 1.04 to 1.22, p<0.001). The risk was also elevated in the male population, hypertensive individuals, glycosylated haemoglobin (HbA1c)≥6.5% and age ≥60 years in the South. Besides the above groups, diabetes was also a risk factor for the Northern population.

**Conclusions** In China, people with both central and peripheral obesity are prone to a high UACR, and the southern population has a higher risk than northern population. Factors such as male sex, hypertension, HbA1c≥6.5% and an age ≥60 years are also risk factors for CKD.

## Strengths and limitations of this study

► This was a cross-sectional study, with multicentre as well as a large sample of 41 085 patients without chronic kidney disease in China.

► Due to the difference in the kit and range of normal values, the urinary albumin-creatinine ratio (UACR) was transferred to quartile, so it could not be expressed as a continuous variable.

► As a cross-sectional study, a causal relationship between obesity and the UACR cannot be established.

► Some of the data such as smoking, drinking habits and drug history are self-reported, so recall bias cannot be avoided.

## INTRODUCTION

Chronic kidney disease (CKD) is defined as chronic kidney structural and functional loss caused by various factors (for 3 months or more), including normal or abnormal pathological damage of glomerular filtration rate (eGFR) as well as abnormal blood, urine and imaging examination, or an unexplained decrease in eGFR ($<60\,\mathrm{mL/min/1.73\,m^2}$) for more than 3 months. CKD has become one of the major chronic diseases with a low rate of awareness.[1 2] In 2012, the prevalence of CKD in China was 10.8%; however, only 12.5% of patients were aware of the disease.[3] It has been proven that CKD is an independent risk factor for cardiovascular disease, and the prognosis of cardiovascular disease in these patients is worse than that of patients without kidney damage.[4] A meta-analysis in 2010 suggested that compared with participants with an eGFR of $95\,\mathrm{mL/min/1.73\,m^2}$, the risk of cardiovascular mortality was significantly increased in participants with lower eGFR.[5]

Obesity has been proven to be one of the most common causes of CKD, leading to a deterioration of structure and function of the kidney, which is characterised as microalbuminuria.[6] Currently, the urinary

albumin-creatinine ratio (UACR) is the most widely used measurement for early screening for microalbuminuria, owing to its accuracy and convenience.[7] Some studies have indicated that obese patients have a higher level of UACR. However, the association between obesity and UACR remains unclear. Recent studies, including those in Japan, Taiwan and Germany, have suggested that obesity is correlated with UACR, while others have not found a correlation.[8–11] Moreover, due to the diversity of eating habits in different regions, the prevalence of obesity varies. In China, vast land areas and long histories have different eating habits, and living customs in the North and South. In 2014, the proportion of overweight and obesity in the southern male of childbearing age was 24.8%, and 43.5% in the North; the proportion in southern women of childbearing age was 13% and that of the northern population was 29.6%.[12] Thus, the association between obesity and UACR may be affected by geographical factors, which has not been previously studied.

In this regard, the study focuses on the relationship between obesity and the UACR, as well as the difference in the North and South of China.

## METHODS
### Study population
A total of 53639 participants from eight regional centres in REACTION (China's Risk Evaluation of cAncers in Chinese diabeTic Individuals, a lONgitudinal study) had written informed consents. Among them, Dalian, Lanzhou and Zhengzhou were the centres of the North; Guangzhou, Guangxi, Luzhou, Shanghai and Wuhan were the centres of the South. The study population included all permanent residents aged over 40 years in 3–5 communities by random sampling of urban areas, with a middle level of economy. These subjects can better represent the urban middle-aged and elderly population. We contacted the community officers of each centre for support and recruited participants who met the criteria through telephone. Inclusion and exclusion criteria: (1) Inclusion criteria: individuals aged over 40 years, without restrictions on gender proportion, having good compliance (being objective and sincere for questionnaires, and being able to accept regular follow-up). (2) Exclusion criteria: patients with confirmed CKD (with clear videography, laboratory and pathology and a duration of disease longer than 3 months); with other kidney diseases that can lead to increased urinary protein excretion, including primary nephropathy and secondary nephropathy; daily use of angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers medicine; with important data missing.

### Data collection
Standardised questionnaires were used to collect information including basic information, medical history, medication history and lifestyle. Measurements included height (H), weight (W), waist circumference (WC), hip circumference (HC) and blood pressure (BP) (systolic and diastolic (SBP, DBP)). Patients were asked to take off shoes, hats and clothes before measurement. Body mass index (BMI)=$W/H^2$ (kg/m$^2$) WC was defined as the circumference of the abdomen of the lower edge of the rib and the midpoint of the sacral line. The HC measure was the maximum circumference of the buttocks. Waist-to-hip ratio (WHR)=WC/HC. Before the BP measurement, patients were required to rest for at least 5 min. Measurement was done thrice with a mercury sphygmomanometer in 1 min, and the average value taken. All investigators had been previously trained.

### Blood biochemical measurement
Blood samples were collected in the morning after subjects were on a fast for at least 8 hours before test. Participants without a history of diabetes mellitus (DM) underwent a 75 g glucose tolerance test, and their venous blood samples were drawn at 0 and 120 min. Biochemical indices included triglyceride (TG), cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), serum creatinine (Scr), blood urea nitrogen, liver function index (alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase), fasting blood glucose (FBG), postprandial blood glucose (PBG), fasting blood insulin (0 min, 120 min) and glycosylated haemoglobin (HbA1c). Fasting blood insulin was measured using the glucose oxidase–peroxidase method.

### UACR measurement and data processing
Urine samples were mid-clean urine collected in the morning. In order to eliminate the data error caused by the difference of the kit and the different ranges of normal values, ln UACR/media (the value of UACR over the median of each centre) was used instead of UACR. According to the quartiles of each centre, UACR data were divided into <25%, 25%–50%, 50%–75% and ≥75% groups.

### Obesity measurements
BMI and WHR were used to measure peripheral obesity and central obesity. According to the Chinese adult BMI standard, BMI ≥28.0 kg/m$^2$ was diagnosed as peripheral obesity. WHR ≥0.9 for males as well as WHR ≥0.85 for females were used to diagnose central obesity. The obesity group was divided into O1 (non-obesity): BMI <28 kg/m$^2$ with WHR below standard; O2 (peripheral obesity): BMI ≥28 kg/m$^2$ with WHR below standard; O3 (central obesity): BMI <28 kg/m$^2$ with WHR over standard; O4 (both peripheral and central obesity): BMI ≥28 kg/m$^2$ with WHR over standard.

### Multiple groups
Multiple groups were used to investigate the relationship between obesity and the UACR in different groups: hypertension group (non-HP: SBP <140 mm Hg and DBP <90 mm Hg, HP: SBP ≥140 mm Hg or DBP ≥90 mm Hg), HbA1c group (HbA1c<6.5%, HbA1c≥6.5%),

glycometabolic group (normal: normal glucose tolerance, pro-DM: pre-DM, DM: diabetes), age group (age <45 years, 45 ≤age <60 years, age ≥60 years) and gender group (male, female). The glycometabolic group was classified by FBG and PBG according to DM diagnostic criteria.

## Statistical analysis
Statistical analysis was performed using SPSS V.23.0. All continuous variables were presented as mean±SD or median (IQR). Categorical variables are presented as numbers (proportions). Normally distributed measurement data were tested by analysis of covariance regression, and non-normally distributed measurement data were tested using a non-parametric test. Enumeration data were tested using the $\chi^2$ test. The comparison between groups of baseline data was performed by Student-Newman -Keuls test. Ordinary logistic regression was used to examine the cross-sectional association between obesity and the UACR. $P<0.05$ was considered statistically significant.

## Patient and public involvement
Patients or the public were not involved in the design, planning or conduct of our research.

## RESULTS
### Baseline information
A total of 41 085 individuals were selected, including 12 697 males and 28 388 females, with 21 213 individuals from the South and 19 872 individuals from North. The baseline data in the South and North are shown in table 1. It could be inferred that the average BMI in the South was lower than that in the North, and there was no significant difference in the average WHR. The proportion of central obesity in the south was higher than North, which was 53.9% over 45.6%, while people with both central and peripheral obesity in the North were higher than those in the South, 15.8% in the North and 8.8% in the South. The factors of male proportion, Scr and ln UACR/media were higher in the South, while the prevalence of various chronic diseases such as hypertension, DM, coronary heart disease (CHD), SBP, DBP, TC, TG, ALT, AST, FBG, PBG and HbA1c were higher in the North (table 1). Baseline data showed that compared with the normal weight group (O1), the obesity groups (O2, O3 and O4) had higher LDL, HDL, FBG, PBG, HbA1c, SBP, DBP, TC, TG, ALT, AST, ln UACR/media and male proportion (p<0.001; tables 2 and 3).

### Trends of UACR in the South and North
ln UACR/media (the value of UACR over median of each centre) was used instead of UACR to show the distribution of UACR in the South and North under obesity groups. Compared with O1 (non-obesity), both O2 (peripheral obesity) and O3 (central obesity) had higher UACR, and UACR levels were significantly elevated in O4 (both peripheral and central obesity). In the North–South comparison, the average level of UACR in each group was higher in the South, both in the non-obesity and obesity groups (p<0.001) (figure 1).

### Correlation between obesity and UACR in the north–south group
Ordinary logistic regression was used to verify the difference between obesity and UACR. With uncorrected factor (model 1) or corrected for gender, age, smoking and drinking (model 2), it can be identified in the total population; obesity was positively associated with UACR, and the risk was higher in O4 (both peripheral and central obesity) than in other groups (p<0.001). Similar findings were obtained in North–South subgroup, especially in the South, where the risk of O4 increased to 1.95 times of O1 (OR: 1.95; 95% CI: 1.78 to 2.14, p<0.001). Moreover, the risk of high UACR in the South was much higher than in the North (p<0.001). By fully adjusting for HbA1c, DBP, TG, AST, sex, age, smoking and drinking (model 3), the relationship between obesity and the UACR in O4 was still significant. However, this association disappeared in O2 and O3, indicating that there is no difference in the development of a high UACR in individuals with either peripheral obesity or central obesity, in contrast with those without obesity. These findings existed both in the total population and in the North–South group. In the comparison of the North–South group, when multivariate factors were adjusted, the risk of a high UACR in the South was still higher than that in the North (OR $_{South}$: 1.22, 95% CI: 1.11 to 1.34; OR $_{North}$: 1.13, 95% CI: 1.04 to 1.22, p<0.001) (table 3).

### Relationship between obesity and UACR in multiple population groups
The results showed that in the South, obesity has a significant association with UACR in the group with HbA1c ≥6.5% and age ≥45 years, especially in the elderly population (age ≥60 years), which showed a positive relationship between obesity and the UACR in both O3 and O4 (OR$_{O3}$: 1.13, 95% CI: 1.02 to 1.24; OR$_{O4}$: 1.31, 95% CI: 1.12 to 1.52, p<0.001). In summary, the risk of a high UACR was elevated in the central obesity group who were older than 60 years. In the North, in addition to above factors, the risk was also higher in people with DM (OR$_{O4}$: 1.23, 95% CI: 1.05 to 1.43, p=0.01). A significant interaction exists between obesity and gender as well as obesity and hypertension. Subsequently, we further divided the population by sex and hypertension to observe the effects of the interaction. This shows that the male population is more closely associated with obesity and the UACR both in the South and North. As for hypertension, stratified analysis showed that SBP ≥140 mm Hg or DBP ≥90 mm Hg was more closely related to obesity and UACR. Moreover, the results also indicate that the risk of high UACR in the South is higher than that in the North for each group (p<0.05) () (tables 4–6).

**Table 1** Comparison of baseline data of different populations in the South and North

| | South (n=21 213) | North (n=19 872) | P value |
|---|---|---|---|
| BMI (kg/m$^2$) | 23.95±3.57 | 25.15±3.72 | <0.001 |
| WHR | | | 0.78 |
| Male | 0.91±0.07 | 0.91±0.06 | |
| Female | 0.87±0.08 | 0.87±0.07 | |
| Obesity groups (%) | | | <0.001 |
| O1 (non-obesity) | 7577 (35.7) | 7068 (35.6) | |
| O2 (peripheral obesity) | 326 (1.5) | 594 (3) | |
| O3 (central obesity) | 11 437 (53.9) | 9067 (45.6) | |
| O4 (both peripheral and central obesity) | 1873 (8.8) | 3143 (15.8) | |
| Age (years) | 58.26±9.81 | 58.02±8.65 | 0.009 |
| Male (%) | 7046 (33.2) | 5651 (28.4) | <0.001 |
| Coronary heart disease (%) | 619 (3.1) | 867 (4.4) | <0.001 |
| Diabetes (%) | 2035 (9.7) | 2356 (11.9) | <0.001 |
| Hypertension (%) | 3922 (19.7) | 3759 (19.0) | 0.09 |
| Hyperlipidaemia (%) | 1411 (7.1) | 1845 (9.3) | <0.001 |
| Smoking habits | | | 0.98 |
| Regularly smoke (%) | 2472 (11.9) | 2339 (11.8) | |
| Sometimes smoke (%) | 495 (2.4) | 487 (2.5) | |
| Never smoke (%) | 17 890 (85.8) | 16 965 (85.7) | |
| Drinking habits | | | 0.01 |
| Regularly drink (%) | 1386 (6.6) | 1365 (6.9) | |
| Sometimes drink (%) | 3789 (18.2) | 3815 (19.3) | |
| Never drink (%) | 15 692 (75.2) | 14 593 (73.8) | |
| HbA1c (%) | 6.03±1.01 | 6.15±1.08 | <0.001 |
| SBP (mm Hg) | 128.75±19.41 | 134.38±21.11 | <0.001 |
| DBP (mm Hg) | 76.54±10.41 | 78.26±11.20 | <0.001 |
| Scr (µmol/L) | 69.08±16.42 | 67.07±15.85 | <0.001 |
| TG (mmol/L) | 1.64±1.23 | 1.69±1.15 | <0.001 |
| TC (mmol/L) | 5.13±1.13 | 5.04±1.12 | <0.001 |
| HDL (mmol/L) | 1.34±0.35 | 1.31±0.32 | <0.001 |
| LDL (mmol/L) | 3.03±0.89 | 2.93±0.89 | <0.001 |
| GGT (mmol/L) | 28.79±38.07 | 30.97±41.14 | <0.001 |
| AST (mmol/L) | 21.67±13.14 | 23.25±11.75 | <0.001 |
| ALT (mmol/L) | 16.47±13.4 | 19.41±14.17 | <0.001 |
| FBG (mmol/L) | 5.81±1.58 | 6.16±1.84 | <0.001 |
| PBG (mmol/L) | 8.22±3.68 | 8.83±4.22 | <0.001 |
| ln UACR/media | 0.13±1.08 | 0.09±1.04 | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 87.59±17.79 | 89.02±17.42 | <0.001 |

Continuous variables were presented as mean±SD or median (IQR), and categorical variables were presented by numbers (proportions).
ALT, alanine amino transferase; AST, aspartate amino transferase; BMI, body mass index; DBP, average diastolic blood pressure; eGFR, glomerular filtration rate; FBG, fasting blood glucose; GGT, glutamyl transpeptidase; HbA1c, glycosylated haemoglobin; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; O1, non-obesity ; O2, peripheral obesity; O3, central obesity; O4, both peripheral and central obesity; PBG, postprandial blood glucose; SBP, average systolic blood pressure; Scr, creatinine; TC, cholesterol; TG, triglyceride; UACR, urinary albumin-creatinine ratio; WHR, waist-to-hip ratio.

**Table 2** Basic characteristics of patients under different obesity groups in the South

| South | O1 (n=7577) | O2 (n=326) | O3 (n=11 437) | O4 (n=1873) | P value |
|---|---|---|---|---|---|
| Age (years) | 55.58±8.75 | 56.01±9.20 | 59.84±10.04 | 59.74±10.07 | <0.001 |
| Male (%) | 2795 (36.9) | 105 (32.2) | 3541 (31.0) | 605 (32.3) | <0.001 |
| Coronary heart disease (%) | 146 (2.1) | 5 (1.7) | 372 (3.5) | 96 (5.6) | <0.001 |
| Diabetes (%) | 467 (6.2) | 17 (5.4) | 1268 (11.2) | 283 (15.3) | <0.001 |
| Hypertension (%) | 797 (11.3) | 76 (25.8) | 2380 (21.9) | 669 (38.1) | <0.001 |
| Hyperlipidaemia (%) | 340 (4.9) | 25 (8.7) | 835 (7.8) | 211 (12.3) | <0.001 |
| Smoking habits | | | | | <0.001 |
| Regularly smoke (%) | 963 (13.0) | 21 (6.5) | 1281 (11.4) | 207 (11.3) | |
| Sometimes smoke (%) | 189 (2.5) | 12 (3.7) | 248 (2.2) | 46 (2.5) | |
| Never smoke (%) | 6282 (84.5) | 288 (89.7) | 9734 (86.4) | 1586 (86.2) | |
| Drinking habits | | | | | <0.001 |
| Regularly drink (%) | 496 (6.7) | 21 (6.6) | 741 (6.6) | 128 (7.0) | |
| Sometimes drink (%) | 1605 (21.6) | 54 (16.9) | 1851 (16.4) | 279 (15.2) | |
| Never drink (%) | 5337 (71.8) | 245 (76.6) | 8676 (77.0) | 1434 (77.9) | |
| HbA1c (%) | 5.86±0.85 | 6.08±0.98 | 6.10±1.09 | 6.31±1.05 | <0.001 |
| SBP (mm Hg) | 123.29±18.07 | 132.21±18.98 | 130.75±19.29 | 138.01±19.51 | <0.001 |
| DBP (mm Hg) | 74.60±10.25 | 79.35±10.10 | 77.01±10.16 | 81.00±10.80 | <0.001 |
| Scr (µmol/L) | 68.81±17.46 | 67.80±13.01 | 69.19±15.81 | 69.60±16.04 | 0.08 |
| TG (mmol/L) | 1.38±1.01 | 1.69±1.11 | 1.75±1.30 | 2.02±1.38 | <0.001 |
| TC (mmol/L) | 5.07±1.14 | 5.11±1.15 | 5.17±1.12 | 5.13±1.13 | <0.001 |
| HDL (mmol/L) | 1.41±0.37 | 1.29±0.34 | 1.31±0.33 | 1.21±0.30 | <0.001 |
| LDL (mmol/L) | 2.96±0.90 | 3.07±0.93 | 3.07±0.89 | 3.08±0.87 | <0.001 |
| GGT (mmol/L) | 25.49±38.62 | 32.03±33.42 | 29.88±38.71 | 34.71±29.43 | <0.001 |
| AST (mmol/L) | 21.12±12.47 | 22.78±11.56 | 21.68±13.41 | 23.57±13.84 | <0.001 |
| ALT (mmol/L) | 14.64±12.45 | 18.26±13.37 | 16.91±13.37 | 20.73±15.61 | <0.001 |
| FBG (mmol/L) | 5.60±1.33 | 5.79±1.33 | 5.88±1.70 | 6.19±1.65 | <0.001 |
| PBG (mmol/L) | 7.57±3.20 | 8.69±3.45 | 8.46±3.90 | 9.41±3.76 | <0.001 |
| ln UACR/media | −0.02±1.01 | 0.11±1.17 | 0.18±1.08 | 0.41±1.26 | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 89.61±17.78 | 89.55±18.33 | 86.37±17.52 | 86.55±18.66 | <0.001 |

Continuous variables were presented as mean±SD or median (IQR), and categorical variables were presented by numbers (proportions).
ALT, alanine amino transferase; AST, aspartate amino transferase; DBP, average diastolic blood pressure; eGFR, glomerular filtration rate; FBG, fasting blood glucose; GGT, glutamyl transpeptidase; HbA1c, glycosylated haemoglobin; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; O1, non-obesity; O2, peripheral obesity; O3, central obesity; O4, both peripheral and central obesity; PBG, postprandial blood glucose; SBP, average systolic blood pressure; Scr, creatinine; TC, cholesterol; TG, triglyceride; UACR, urinary albumin-creatinine ratio.

## DISCUSSION

Studies have shown that more than 80% of type 2 DM can be attributed to obesity, which is also associated with an increased risk of CHD.[13] [14] In China, with the improvement of economic conditions, the rate of being overweight and obesity has accelerated in recent years. In 2002, the proportion of overweight and obesity in China was 17.3%; however, in 2014, the proportion of overweight and obesity in males reached 33.8% and 24.8%, respectively.[15] [16] Obesity has replaced famine as a major cause of death worldwide. A meta-analysis showed that in Europe and the USA, the lowest overall mortality rate among people is in the BMI range of 22.5–25 kg/m$^2$. On

this basis, for every 5 kg/m$^2$ increase in BMI, the overall mortality rate will increase by 30%.[17] An article published in New England reported that being overweight and obese could lead to an increase in all-cause mortality and cardiovascular mortality. The current human life expectancy may be terminated owing to an increase in overweight and obesity cases.[18] Numerous large-scale clinical studies have shown that obesity is also associated with CKD, which is a microvascular complication of DM. In 1974, Professor Weisinger reported on four patients with nephrotic syndrome caused by severe obesity, whose pathology mainly showed focal glomerulosclerosis and glomerular enlargement. This kidney disease is called

**Table 3** Basic characteristics of patients under different obesity groups in the North

| North | O1 (7068) | O2 (594) | O3 (9067) | O4 (3143) | P value |
|---|---|---|---|---|---|
| Age (years) | 56.63±8.38 | 58.05±8.44 | 58.64±8.65 | 59.31±8.86 | <0.001 |
| Male (%) | 2154 (30.5) | 186 (31.3) | 2361 (26.0) | 950 (30.2) | <0.001 |
| Coronary heart disease (%) | 210 (3.0) | 29 (4.9) | 409 (4.5) | 219 (7.0) | <0.001 |
| DM (%) | 585 (8.3) | 62 (10.5) | 1216 (13.4) | 493 (15.7) | <0.001 |
| Hypertension (%) | 877 (12.4) | 145 (24.5) | 1765 (19.5) | 972 (31.1) | <0.001 |
| Hyperlipidaemia (%) | 459 (6.5) | 66 (11.2) | 906 (10.0) | 414 (13.3) | <0.001 |
| Smoking habits | | | | | 0.02 |
| Regularly smoke (%) | 897 (12.7) | 57 (9.6) | 1020 (11.3) | 365 (11.6) | |
| Sometimes smoke (%) | 191 (2.7) | 13 (2.2) | 207 (2.3) | 76 (2.4) | |
| Never smoke (%) | 5949 (84.5) | 523 (88.2) | 7799 (86.4) | 2694 (85.9) | |
| Drinking habits | | | | | <0.001 |
| Regularly drink (%) | 452 (6.4) | 38 (6.4) | 608 (6.7) | 267 (8.5) | |
| Sometimes drink (%) | 1536 (21.8) | 113 (19.1) | 1631 (18.1) | 535 (17.1) | |
| Never drink (%) | 5050 (71.8) | 441 (74.5) | 6776 (75.2) | 2326 (74.4) | |
| HbA1c (%) | 5.96±0.90 | 6.10±0.96 | 6.22±1.15 | 6.40±1.16 | <0.001 |
| SBP (mm Hg) | 128.47±19.84 | 139.83±19.99 | 135.57±20.87 | 143.22±20.83 | <0.001 |
| DBP (mm Hg) | 76.1±10.9 | 81.42±11.00 | 78.31±11.10 | 82.35±10.98 | <0.001 |
| Scr (μmol/L) | 67.35±15.99 | 68.18±15.51 | 66.52±15.46 | 67.72±16.60 | <0.001 |
| TG (mmol/L) | 1.47±0.97 | 1.74±1.12 | 1.77±1.22 | 1.96±1.24 | <0.001 |
| TC (mmol/L) | 4.88±1.09 | 5.13±1.11 | 5.10±1.14 | 5.17±1.12 | <0.001 |
| HDL (mmol/L) | 1.35±0.33 | 1.27±0.29 | 1.31±0.33 | 1.23±0.28 | <0.001 |
| LDL (mmol/L) | 2.80±0.86 | 3.06±0.91 | 2.98±0.91 | 3.08±0.90 | <0.001 |
| GGT (mmol/L) | 27.34±41.81 | 33.13±33.75 | 31.63±41.26 | 36.77±39.45 | <0.001 |
| AST (mmol/L) | 22.57±12.19 | 24.46±11.53 | 25.05±12.24 | 22.57±12.19 | <0.001 |
| ALT (mmol/L) | 17.63±13.26 | 22.25±17.20 | 19.26±13.29 | 23.33±16.83 | <0.001 |
| FBG (mmol/L) | 6.11±1.51) | 6.24±1.92 | 6.63±2.11 | 5.85±1.57 | <0.001 |
| PBG (mmol/L) | 7.99±3.70 | 8.82±3.84 | 9.12±3.84 | 9.88±4.41 | <0.001 |
| ln UACR/media | −0.36±1.03 | 0.12±1.09 | 0.11±1.03 | 0.29±1.07 | <0.001 |
| eGFR (mL/min/1.73 m$^2$) | 89.45±17.32 | 88.16±16.96 | 88.94±17.25 | 88.46±18.22 | <0.001 |

Continuous variables were presented as mean±SD or median (IQR) and categorical variables were presented by numbers (proportions).
ALT, alanine amino transferase; AST, aspartate amino transferase; DBP, average diastolic blood pressure; DM, diabetes mellitus; eGFR, glomerular filtration rate; FBG, fasting blood glucose; GGT, glutamyl transpeptidase; HbA1c, glycosylated haemoglobin; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; O1, non-obesity; O2, peripheral obesity; O3, central obesity; O4, both peripheral and central obesity; PBG, postprandial blood glucose; SBP, average systolic blood pressure; Scr, creatinine; TC, cholesterol; TG, triglyceride; UACR, urinary albumin-creatinine ratio.

obesity-related glomerulopathy.[19] An increasing number of studies indicate that obesity is involved in the progression of CKD, but has also proved to be an independent risk factor for renal failure.[20–22]

In recent years, some cohort studies have suggested that obesity has a certain association with UACR, but the conclusions drawn were different and had no correlation. A study of 1990 subjects for a middle-aged male population in 2010 in Japan claimed only WC has a correlation with UACR, while BMI does not have statistical significance.[9] Research undertaken on 12 672 hypertensive patients at the Southern Medical University showed that only BMI is associated with the UACR, whereas WC has

no correlation.[23] In 2014, a study by Suzhou University involving 2889 participants and concluded that both BMI and WHR exceeding the standard are risk factors for a high UACR.[24] Sun Yat-sen University reported that an increase in BMI and WC is associated with the UACR in persons aged over 40 years.[25] All the above studies illustrated that obesity was a risk factor for elevated UACR, but a study of 3979 people in non-diabetic, non-hypertensive patients in Korea announced that the correlation only existed in low BMI (BMI<18.5 kg/m$^2$).[10] A study of 3749 data in Germany yielded a U-shaped curve of obesity and the UACR, indicating that people with weight loss and obesity have a significantly increased risk of a high
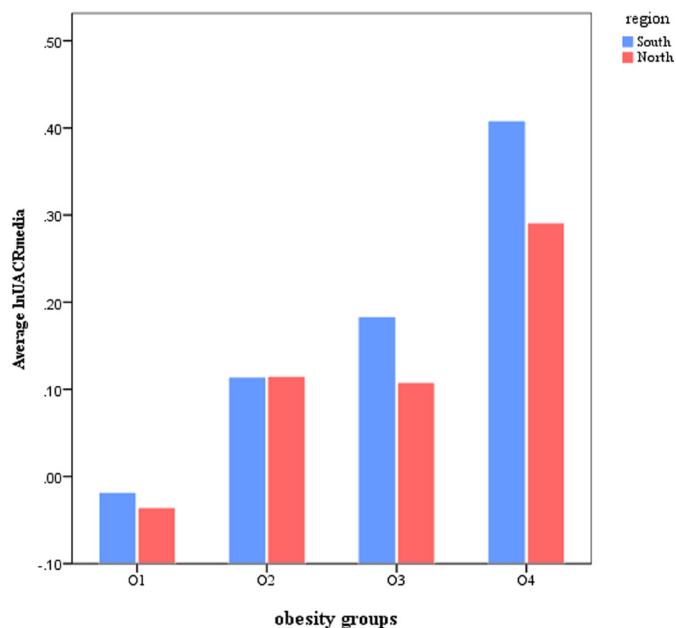
**Figure 1** Distribution of UACR in the South and North: In UACR/median (the value of UACR over median of each centre) was used to show the difference of the average UACR in each obesity group and the comparison between the North and South. UACR, urinary albumin-creatinine ratio.

UACR.[11] With regard to the above studies, there was no uniform conclusion between BMI and WC (or WHR), which may be related to the geographical, ethnic, sample size, gender, age and inclusion–exclusion criteria as well as the correction factors used in the various studies.[26]

Our research showed that compared with non-obese people, patients with both central and peripheral obesity had a risk of a higher UACR, while for those with only peripheral obesity or central obesity, there was no positive relationship. This result remained significant even after adjusting for multiple factors, explaining that obesity was an independent risk factor for high UACR. The results indicated that it might be possible to prevent urinary protein by controlling body weight (ie, maintaining diets, exercise or weight loss surgery),[27–30] but specific mechanisms of weight loss that delay the progression of CKD have not been completely explored. We will continue to focus on further follow-up observations to verify this conclusion.

A study also confirmed that a regional difference exists for the risk of a high UACR. Cheng studied 208 individuals from the South and 109 from the North, and reported that HLA-A*02 alleles possess high heterogeneity and genetic diversity in the Chinese Han population; this verifies that one of the reasons for the regional difference may originate from genetic diversity.[31] Another possible reason may be related to environmental discrepancies. Obesity is a disease easily affected by environment. Owing to its long history and vast territory, China has formed a different geographical environment and climate, which affects the diet and living habits of people in the South and North. These distinctive diets cause a different prevalence of obesity between the two regions, and may affect the relationship between obesity and UACR. Our study indicated that the risk of a high UACR in the South was greater than that in the North, which was not found in

**Table 4** Correlation between obesity and UACR in total population and the North–South group

| | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| Total population | OR (95% CI) | P value | OR (95% CI) | P value | OR (95% CI) | P value |
| O1 (14645) | 1 | | 1 | | 1 | |
| O2 (920) | 1.28 (1.14 to 1.44) | <0.001 | 1.22 (1.08 to 1.38) | <0.001 | 1.04 (0.92 to 1.17) | 0.16 |
| O3 (20504) | 1.28 (1.23 to 1.33) | <0.001 | 1.11 (1.06 to 1.15) | <0.001 | 0.98 (0.94 to 1.02) | 0.34 |
| O4 (5016) | 1.72 (1.62 to 1.82) | <0.001 | 1.50 (1.41 to 1.59) | <0.001 | 1.14 (1.07 to 1.21) | <0.001 |
| South | | | | | | |
| O1 (7577) | 1 | | 1 | | 1 | |
| O2 (326) | 1.32 (1.08 to 1.61) | 0.01 | 1.30 (1.07 to 1.59) | 0.01 | 1.12 (0.91 to 1.37) | 0.28 |
| O3 (11437) | 1.35 (1.28 to 1.42) | <0.001 | 1.14 (1.08 to 1.20) | <0.001 | 1.03 (0.97 to 1.08) | 0.37 |
| O4 (1873) | 1.95 (1.78 to 2.14) | <0.001 | 1.66 (1.51 to 1.82) | <0.001 | 1.22 (1.11 to 1.34) | <0.001 |
| North | | | | | | |
| O1 (7068) | 1 | | 1 | | 1 | |
| O2 (594) | 1.24 (1.07 to 1.44) | 0.001 | 1.18 (1.02 to 1.38) | 0.03 | 1.07 (0.92 to 1.24) | 0.42 |
| O3 (9067) | 1.20 (1.13 to 1.26) | <0.001 | 1.07 (1.02 to 1.14) | 0.01 | 1.01 (0.95 to 1.07) | 0.72 |
| O4 (3143) | 1.56 (1.45 to 1.69) | <0.001 | 1.41 (1.30 to 1.52) | <0.001 | 1.13 (1.04 to 1.22) | <0.001 |

Model 1: uncorrected; model 2: correcting for gender, age, smoking, drinking; model 3: correcting for gender, age, smoking, drinking, HbA1c, DBP, TG and AST.
AST, aspartate aminotransferase; DBP, diastolic blood pressure; HbA1c, glycosylated haemoglobin; O1, non-obesity; O2, peripheral obesity; O3, central obesity; O4, both peripheral and central obesity; TG, triglyceride; UACR, urinary albumin-creatinine ratio.

**Table 5** Correlation between obesity and UACR in different population groups in the South

| South | O1 (7577) OR (95% CI) | P value | O2 (326) OR (95% CI) | P value | O3 (11437) OR (95% CI) | P value | O4 (1873) OR (95% CI) | P value | P value for interaction |
|---|---|---|---|---|---|---|---|---|---|
| Hypertension (mm Hg) | | | | | | | | | 0.05 |
| Non-HP | 1 | | 1.00 (0.78 to 1.28) | 0.99 | 1.00 (0.94 to 1.07) | 0.89 | 1.23 (1.08 to 1.39) | <0.001 | |
| HP | 1 | | 1.28 (0.90 to 1.82) | 0.18 | 1.05 (0.93 to 1.18) | 0.42 | 1.29 (1.10 to 1.51) | <0.001 | |
| HbA1c (%) | | | | | | | | | 0.4 |
| <6.5 | 1 | | 1.00 (0.80 to 1.25) | 0.99 | 0.99 (0.93 to 1.05) | 0.63 | 1.19 (1.07 to 1.33) | <0.001 | |
| ≥6.5 | 1 | | 1.52 (0.91 to 2.55) | 0.11 | 1.02 (0.87 to 1.20) | 0.84 | 1.30 (1.05 to 1.62) | 0.02 | |
| Age (years) | | | | | | | | | 0.97 |
| ≤45 | 1 | | 1.07 (0.58 to 1.95) | 0.84 | 1.17 (0.97 to 1.42) | 0.1 | 1.21 (1.83 to 1.75) | 0.32 | |
| 45–60 | 1 | | 0.95 (0.72 to 1.24) | 0.72 | 0.96 (0.89 to 1.03) | 0.23 | 1.25 (1.09 to 1.43) | <0.001 | |
| ≥60 | 1 | | 1.21 (0.84 to 1.74) | 0.31 | 1.13 (1.02 to 1.24) | 0.02 | 1.31 (1.12 to 1.52) | <0.001 | |
| Gender | | | | | | | | | <0.001 |
| Male | 1 | | 1.05 (0.73 to 1.50) | 0.79 | 0.96 (0.87 to 1.05) | 0.36 | 1.39 (1.18 to 1.64) | <0.001 | |
| Female | 1 | | 1.07 (0.84 to 1.37) | 0.58 | 1.01 (0.94 to 1.08) | 0.88 | 1.16 (1.03 to 1.30) | 0.02 | |

Hypertension (HP: SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg, non-HP: SBP <140 mm Hg and DBP < 90 mm Hg), HbA1c (HbA1c < 6.5%, HbA1c ≥ 6.5%), age (age<45, 45≤age<60, age≥60), gender (male, female).
DBP, diastolic blood pressure; HbA1c, glycosylated haemoglobin; HP, hypertension; O1, non-obesity; O2, peripheral obesity; O3, central obesity; O4, both peripheral and central obesity; SBP, average systolic blood pressure; UACR, urinary albumin-creatinine ratio.

**Table 6** Correlation between obesity and UACR in different population groups in the North

| North | O1 (7068) OR (95% CI) | P value | O2 (594) OR (95% CI) | P value | O3 (9067) OR (95% CI) | P value | O4 (3143) OR (95% CI) | P value | P value for interaction |
|---|---|---|---|---|---|---|---|---|---|
| Hypertension (mm Hg) | | | | | | | | | 0.01 |
| Non-HP | 1 | | 1.06 (0.87 to 1.31) | 0.56 | 0.94 (0.88 to 1.01) | 0.08 | 0.96 (0.86 to 1.08) | 0.51 | |
| HP | 1 | | 1.09 (0.86 to 1.37) | 0.47 | 1.03 (0.93 to 1.14) | 0.62 | 1.31 (1.16 to 1.48) | <0.001 | |
| HbA1c (%) | | | | | | | | | 0.22 |
| <6.5 | 1 | | 1.06 (0.90 to 1.25) | 0.5 | 0.97 (0.91 to 1.03) | 0.35 | 1.14 (1.04 to 1.25) | 0.01 | |
| ≥6.5 | 1 | | 1.10 (0.76 to 1.60) | 0.61 | 1.04 (0.90 to 1.21) | 0.6 | 1.20 (1.01 to 1.42) | 0.04 | |
| Glycometabolic | | | | | | | | | 0.26 |
| Normal | 1 | | 1.12 (0.88 to 1.40) | 0.37 | 0.93 (0.86 to 1.00) | 0.06 | 1.13 (1.00 to 1.29) | 0.16 | |
| Pro-DM | 1 | | 0.95 (0.74 to 1.24) | 0.71 | 0.96 (0.86 to 1.07) | 0.47 | 1.11 (0.96 to 1.27) | 0.15 | |
| DM | 1 | | 1.12 (0.81 to 1.54) | 0.52 | 1.16 (1.02 to 1.32) | 0.03 | 1.23 (1.05 to 1.43) | 0.01 | |
| Age (years) | | | | | | | | | 0.31 |
| ≤45 | 1 | | 1.07 (0.59 to 1.95) | 0.82 | 1.13 (0.89 to 1.42) | 0.31 | 1.04 (0.74 to 1.47) | 0.81 | |
| 45–60 | 1 | | 1.00 (0.81 to 1.23) | 1 | 0.96 (0.89 to 1.04) | 0.33 | 1.09 (0.98 to 1.21) | 0.12 | |
| ≥60 | 1 | | 1.07 (0.84 to 1.36) | 0.59 | 0.97 (0.88 to 1.06) | 0.48 | 1.22 (1.07 to 1.38) | <0.001 | |
| Gender | | | | | | | | | <0.001 |
| Male | 1 | | 1.02 (0.78 to 1.35) | 0.87 | 0.95 (0.86 to 1.06) | 0.41 | 1.21 (1.05 to 1.40) | 0.01 | |
| Female | 1 | | 1.07 (0.89 to 1.28) | 0.51 | 0.97 (0.91 to 1.04) | 0.42 | 1.11 (1.01 to 1.22) | 0.04 | |

DM, diabetes mellitus; HbA1c, glycosylated haemoglobin; HP, hypertension; O1, non-obesity; O2, peripheral obesity; O3, central obesity; O4, both peripheral and central obesity; UACR, urinary albumin-creatinine ratio.

previous studies. First, the baseline data showed that the average UACR of the South was higher than that of the North, suggesting that the overall prevalence of a high UACR is greater in the South. Second, the rate of overall obesity (central and peripheral obesity) in the North was higher than that in the South, while the rate of central obesity in the South was significantly higher than North (central obesity ratio was 53.9% in the South and 45.6% in the North). Many studies have shown that central obesity has a higher risk of an elevated UACR than peripheral obesity, which may explain why the risk was higher in the South.[32 33] Moreover, the southern population had a lower average obesity rate than the northern population, making it easier for them to exceed obesity standards. Therefore, it is more dangerous to gain the same weight or WC as the northern population.

A stratified population study showed that the risk of a high UACR was significantly increased in people with hypertension. Hypertension is a proven aetiology of CKD. A study by Southern Medical University, including 12 672 hypertensive patients, suggested that in the hypertensive population, obesity was related to the UACR. However, only BMI was statistically significant, while WC was not significantly different.[22 23] Our study also concluded that in patients with hypertension, who had both central and peripheral obesity, the relationship between a high UACR and obesity was positive. Moreover, the results of the interaction also indicate that hypertension is a stronger factor affecting the relationship between obesity and the UACR. In the non-HP (normal BP group) of the North, no correlation was found between obesity and the UACR, which also indicated that hypertension plays an important role in the development of CKD.

The study also found that the relationship between obesity and the UACR significantly increased in patients with high glycated haemoglobin levels. DM has been confirmed to be one of the causes of CKD. Tomomichi Koshi showed that elevated HbA1c, but not FBG, could identify CKD risk in non-diabetic individuals.[34] Huang also suggested that HbA1c, not FBG or PBG, was independently associated with an increased risk of low-grade albuminuria in middle-aged and elderly Chinese individuals.[35] The above studies both used eGFR as a measure of CKD, while our study focused on UACR and people without CKD, which can be more precise in terms of responding to early renal impairment. This indicates that high HbA1c levels as well as FBG and PBG play an important role in CKD; therefore, early screening and control of these factors of DM may help to prevent CKD.

Unexpectedly, we found a positive association between the UACR and central obesity in people over 60 years old in the South, which did not exist in any other groups, suggesting that senescence may be a stronger factor than obesity for CKD. Polkinghorne et al verified in a study of 17 762 participants, with an average age of 75.1 years, that increasing age was the factor most strongly associated with the presence of CKD, which was similar to our study.[36] However, the study of Polkinghorne focused on

the elderly population and did not clearly define the age level. Our study was established in people without CKD, and the age group was further divided according to clinical criteria, indicating that age over 60 years is a strong risk factor for early CKD. Thus, early screening should be conducted among people over 60 years of age.

The study also suggested the role of gender, showing that males are more vulnerable than females. Some research showed that male sex was an independent factor for CKD. A study from Central South University, which included 26 655 patients, found that obesity was associated with the UACR in the male population, but not in women.[37] Further, studies from France and Japan also emphasised similar gender differences in that only males were at risk for CKD.[38 39] The above conclusions were similar to those of our study, but we also found a positive correlation in females, although the risk was lower than that in males. In addition, the interaction between obesity and gender also suggested that males might have a deeper impact on the relationship. One of the reasons may be related to the participants that we recruited, which were 2/3 females. Another may be related to the different ethnicities of each study. The mechanism by which the risk of high UACR in females was lower than in males may be related to the protective effects of oestrogen.[40] Oestrogen has antioxidant properties that can reduce the proliferation of mesangial cells and delay glomerular fibrosis,[41 42] while androgens may alter renal haemodynamics by activating the renin–angiotensin–aldosterone system.[43] However, current research cannot fully explain this phenomenon, and further research is needed.

There are some conclusions about the mechanism of why obesity is related to chronic kidney damage. Obesity, especially abdominal obesity, can lead to an increase in visceral fat and physical pressure in the kidney, which may cause kidney compression and increase renal capacity load. Owing to the increased volumetric load, renal blood flow increases as well, and in the early stages, it can improve eGFR. However, if the glomerular vessel wall and endothelial cells remain in this state, high perfusion will stiffen the blood vessel wall and glomerular fibrosis, which eventually causes a decrease in the eGFR. This mechanism can correspond to the clinical eGFR stage of CKD, and can also be observed in non-hypertensive patients with obesity, suggesting that obesity is an independent risk factor for CKD.[19 44] Excessive lipid deposition in kidney tissue is also one of the factors that may lead to mitochondrial dysfunction, apoptosis, induction of oxidative stress and ultimately damage to glomerular filtration membrane podocytes, resulting in glomerular sclerosis and tubular fibrosis.[45 46] Other factors include activation of sympathetic–renin–angiotensin, involvement of insulin resistance, metabolic disorders and infection.[6 47 48] However, the specific mechanisms of the factors remain unclear; thus, more elaborate experimental evidence is required.

The research was conducted based on a multicentre and large sample size study, followed by random sampling

standard, strict inclusion and exclusion standards and a unified investigation method. Moreover, we controlled for possible related factors that may influence the association in order to delete confounding factors. Thus, the results are reliable and convincing. However, there may be some factors affecting the accuracy of the results. Not all possible related factors could be measured during investigation, and some intermediate variables may exist between the relationship of obesity and the UACR. Some limitations cannot be ignored in the study. First, as a cross-sectional study, the causal relationship between obesity and the UACR cannot be established. Second, due to the difference of the kit and range of normal values, UACR was transferred to quartile, so it could not be defined as a clinical standard. Third, the study was conducted in a middle-aged and elderly Chinese population, which could limit its generalisability to other ages and ethnicities. Moreover, some of the data such as smoking, drinking habits and medicine history are self-reported, so recall bias cannot be avoided. Thus, it is necessary to further explore the association between obesity and the UACR by prospective follow-up studies.

## CONCLUSION

The present study showed that obesity is an independent risk factor for elevated UACR. Patients with both central and peripheral obesity have a greater risk for high UACR than those with normal weight, and the risk in the South is higher than that in the North in China. Multiple factors such as hypertension, high glycated haemoglobin and advanced age are also risk factors for a high UACR. These conclusions suggest that controlling weight in these persons may be related to the prevention of CKD.

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## REFERENCES

1. Webster AC, Nagler EV, Morton RL, *et al*. Chronic kidney disease. *Lancet* 2017;389:1238–52.
2. Hall ME, do Carmo JM, da Silva AA, *et al*. Obesity, hypertension, and chronic kidney disease. *Int J Nephrol Renovasc Dis* 2014;7:75–88.
3. Zhang L, Wang F, Wang L, *et al*. Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet* 2012;379:815–22.
4. Nichols GA, Déruaz-Luyet A, Hauske SJ, *et al*. The association between estimated glomerular filtration rate, albuminuria, and risk of cardiovascular hospitalizations and all-cause mortality among patients with type 2 diabetes. *J Diabetes Complications* 2018;32:291–7.
5. Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, *et al*. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010;375:2073–81.
6. Garland JS. Elevated body mass index as a risk factor for chronic kidney disease: current perspectives. *Diabetes Metab Syndr Obes* 2014;7:347–55.
7. Smith ER, Cai MMX, McMahon LP, *et al*. The value of simultaneous measurements of urinary albumin and total protein in proteinuric patients. *Nephrol Dial Transplant* 2012;27:1534–41.
8. Minoo F, Mahdavi-Mazdeh M, Abbasi M-R, *et al*. Impact of the severity of obesity on microalbuminuria in obese normotensive nondiabetic individuals. *J Renal Inj Prev* 2015;4:34–8.
9. Tamba S, Nakatsuji H, Kishida K, *et al*. Relationship between visceral fat accumulation and urinary albumin-creatinine ratio in middle-aged Japanese men. *Atherosclerosis* 2010;211:601–5.
10. Seo W-J, Lee G-M, Hwang J-H, *et al*. Association between body mass index, waist circumference and prevalence of microalbuminuria in Korean adults of age 30 years and older without diabetes, hypertension, renal failure, or overt proteinuria: the 2013 Korean National health and nutrition examination survey. *Korean J Fam Med* 2016;37:57–63.
11. Dittmann K, Hannemann A, Wallaschofski H, *et al*. U-shaped association between central body fat and the urinary albumin-to-creatinine ratio and microalbuminuria. *BMC Nephrol* 2013;14:87.

12 He Y, Pan A, Yang Y, *et al*. Prevalence of underweight, overweight, and obesity among reproductive-age women and adolescent girls in rural China. *Am J Public Health* 2016;106:2103–10.

13 Hruby A, Hu FB. The epidemiology of obesity: a big picture. *Pharmacoeconomics* 2015;33:673–89.

14 Wang Y, Mi J, Shan X-Y, *et al*. Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. *Int J Obes* 2007;31:177–88.

15 He Y, Pan A, Wang Y, *et al*. Prevalence of overweight and obesity in 15.8 million men aged 15-49 years in rural China from 2010 to 2014. *Sci Rep* 2017;7:5012.

16 Wu Y. Overweight and obesity in China. *BMJ* 2006;333:362–3.

17 Scaglione R, Argano C, Di Chiara T, *et al*. Obesity and cardiovascular risk: the new public health problem of worldwide proportions. *Expert Rev Cardiovasc Ther* 2004;2:203–12.

18 Olshansky SJ, Passaro DJ, Hershow RC, *et al*. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med* 2005;352:1138–45.

19 Kambham N, Markowitz GS, Valeri AM, *et al*. Obesity-related glomerulopathy: an emerging epidemic. *Kidney Int* 2001;59:1498–509.

20 Wahba IM, Mak RH. Obesity and obesity-initiated metabolic syndrome: mechanistic links to chronic kidney disease. *Clin J Am Soc Nephrol* 2007;2:550–62.

21 Vivante A, Golan E, Tzur D, *et al*. Body mass index in 1.2 million adolescents and risk for end-stage renal disease. *Arch Intern Med* 2012;172:1644–50.

22 Kramer H, Gutiérrez OM, Judd SE, *et al*. Waist circumference, body mass index, and ESRD in the REGARDS (reasons for geographic and racial differences in stroke) study. *Am J Kidney Dis* 2016;67:62–9.

23 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.

24 Du N, Peng H, Chao X, *et al*. Interaction of obesity and central obesity on elevated urinary albumin-to-creatinine ratio. *PLoS One* 2014;9:e98926.

25 Ren M, Sun K, Li F, *et al*. Association between obesity measures and albuminuria: a population-based study. *J Diabetes Complications* 2016;30:451–6.

26 Wang F, He K, Wang J, *et al*. Prevalence and risk factors for CKD: a comparison between the adult populations in China and the United States. *Kidney Int Rep* 2018;3:1135–43.

27 Chang A, Van Horn L, Jacobs DR, *et al*. Lifestyle-related factors, obesity, and incident microalbuminuria: the cardia (coronary artery risk development in young adults) study. *Am J Kidney Dis* 2013;62:267–75.

28 Chung H-F, Al Mamun A, Huang M-C, *et al*. Obesity, weight change, and chronic kidney disease in patients with type 2 diabetes mellitus: a longitudinal study in Taiwan. *J Diabetes* 2017;9:983–93.

29 Morales E, Valero MA, León M, *et al*. Beneficial effects of weight loss in overweight patients with chronic proteinuric nephropathies. *Am J Kidney Dis* 2003;41:319–27.

30 Chang AR, Chen Y, Still C, *et al*. Bariatric surgery is associated with improvement in kidney outcomes. *Kidney Int* 2016;90:164–71.

31 Cheng L-H, Jin S-Z, Gao S-Q, *et al*. [Difference in HLA-A*02 allele distribution between Han populations in south and north China]. *Di Yi Jun Yi Da Xue Xue Bao* 2005;25:321–4.

32 Cao Y, Sun G, Liu R, *et al*. Plasma triglyceride levels and central obesity predict the development of kidney injury in Chinese community older adults. *Ren Fail* 2019;41:946–53.

33 Bonnet F, Marre M, Halimi J-M, *et al*. Waist circumference and the metabolic syndrome predict the development of elevated albuminuria in non-diabetic subjects: the DESIR study. *J Hypertens* 2006;24:1157–63.

34 Koshi T, Sagesaka H, Sato Y, *et al*. Elevated haemoglobin A1c but not fasting plasma glucose conveys risk of chronic kidney disease in non-diabetic individuals. *Diabetes Res Clin Pract* 2018;146:233–9.

35 Huang X, Zhou Y, Xu B, *et al*. Glycated haemoglobin A1c is associated with low-grade albuminuria in Chinese adults. *BMJ Open* 2015;5:e007429.

36 Polkinghorne KR, Wolfe R, Jachno KM, *et al*. Prevalence of chronic kidney disease in the elderly using the aspirin in reducing events in the elderly study cohort. *Nephrology* 2019;24:1248–56.

37 Liu J, Chen Z, Li W, *et al*. Obesity indices for prediction of chronic kidney disease: a cross-sectional study in 26 655 Chinese adults. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2016;41:445–54.

38 Ishizaka N, Ishizaka Y, Toda E-I, *et al*. Association between obesity and chronic kidney disease in Japanese: differences in gender and hypertensive status? *Hypertens Res* 2007;30:1059–64.

39 de Hauteclocque A, Ragot S, Slaoui Y, *et al*. The influence of sex on renal function decline in people with type 2 diabetes. *Diabet Med* 2014;31:1121–8.

40 Kwan G, Neugarten J, Sherman M, *et al*. Effects of sex hormones on mesangial cell proliferation and collagen synthesis. *Kidney Int* 1996;50:1173–9.

41 Yuan W-J, Jia F-Y, Meng J-Z. Effects of genistein on secretion of extracellular matrix components and transforming growth factor beta in high-glucose-cultured rat mesangial cells. *J Artif Organs* 2009;12:242–6.

42 Reckelhoff JF, Hennington BS, Moore AG, *et al*. Gender differences in the renal nitric oxide (NO) system: dissociation between expression of endothelial NO synthase and renal hemodynamic response to NO synthase inhibition. *Am J Hypertens* 1998;11:97–104.

43 Reckelhoff JF, Granger JP. Role of androgens in mediating hypertension and renal injury. *Clin Exp Pharmacol Physiol* 1999;26:127–31.

44 Henegar JR, Bigler SA, Henegar LK, *et al*. Functional and structural changes in the kidney in the early stages of obesity. *J Am Soc Nephrol* 2001;12:1211–7.

45 Unger RH, Scherer PE. Gluttony, sloth and the metabolic syndrome: a roadmap to lipotoxicity. *Trends Endocrinol Metab* 2010;21:345–52.

46 Thethi T, Kamiyama M, Kobori H. The link between the renin-angiotensin-aldosterone system and renal injury in obesity and the metabolic syndrome. *Curr Hypertens Rep* 2012;14:160–9.

47 Furukawa S, Fujita T, Shimabukuro M, *et al*. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest* 2004;114:1752–61.

48 Sarafidis PA. Obesity, insulin resistance and kidney disease risk: insights into the relationship. *Curr Opin Nephrol Hypertens* 2008;17:450–6.