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Association between obesity measures and albuminuria: A population-based study

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ABSTRACT

Aims: The effects of obesity on the micro vascular diseases have drawn much attention. The aim of the study was to investigate the relationship between obesity measures and albuminuria in Chinese population.
Methods: We conducted a population-based cross-sectional study in 8600 subjects aged 40 years or older from a community in Guangzhou. Urinary albumin excretion and creatinine were measured and urinary albumin-to-creatinine ratio (ACR) was calculated as urinary albumin divided by creatinine. Low-grade albuminuria was classified as the highest quartile of ACR in participants without increased urinary albumin excretion. Increased urinary albumin excretion was defined according to the ACR ranges greater or equal than 30 mg/g.
Results: Pearson's correlation analysis and multivariate linear regression analysis revealed that body mass index (BMI), waist circumference and body fat content were significantly correlated with ACR (all $P < 0.01$). Prevalence of low-grade albuminuria and increased urinary albumin excretion gradually increased across the BMI, waist circumference and body fat content quartiles (all P for trend < 0.0001). Compared with participants in quartile 1 of BMI, waist circumference and body fat content, participants in quartile 4 had increased prevalence of low-grade albuminuria and increased urinary albumin excretion in logistic regression analysis after adjustment for age, sex, physical activity, fasting plasma glucose, triglycerides, low-density lipoprotein cholesterol and HbA1c (all $P < 0.05$).
Conclusion: Obesity measures are associated with urinary albumin excretion in middle-aged and elderly Chinese.

1. Introduction

Increased urinary albumin excretion includes historical micro- and macro-albuminuria, which has been defined as urinary albumin–creatinine ratio (ACR) higher than 30 mg/g (Anonymous, 2013). Until now, many studies have provided substantial evidence of increased urinary albumin excretion as a risk factor for future cardiovascular events (Deckert, Feldt-Rasmussen, Borch-Johnsen, Jensen, & Kofoed-Enevoldsen, 1989; de Zeeuw et al., 2004; Gerstein et al., 2001). Urinary albumin was considered to be a continuous risk marker of cardiovascular disease with no lower limit (Hillege et al., 2002), and every 0.4 mg/mmol (equivalent to 3.01 mg/g) increment in ACR conferred a 5.9% increase of major cardiovascular events (Valmadrid, Klein, Moss, & Klein, 2000). Recently the importance of low-grade albuminuria (ACR less than 30 mg/g) raised concerns. Low-grade albuminuria within the accepted normal range is associated with higher cardiovascular risk (Katz et al., 2014) and might also increase the risk of cardiovascular morbidity and mortality (Arnlov et al., 2005; Ingelsson et al., 2007). Urinary albumin excretion in diabetic patients is generally higher than the level measured in normal individuals (Jensen, Borch-Johnsen, Feldt-Rasmussen, Appleyard, & Jensen, 1997; Jensen et al., 1997). Furthermore, even in healthy individuals without diabetes or hypertension, small amounts of albumin excreted in the urine predict an increased risk of cardiovascular diseases.

Obesity is a metabolic disorder of increasing prevalence worldwide and a risk factor for the development of metabolic syndrome, insulin resistance, type 2 diabetes and endothelial dysfunction (Esser, Legrand-Poels, Piette, Scheen, & Paquot, 2014; Bastard et al., 2006; Heilbronn & Campbell, 2008; Hui, Xu, Bo Yang, & Lam, 2013). Recently, a cross-sectional study in China was conducted to investigate the association between low-grade albuminuria and metabolic syndrome (Zhang et al., 2013). However, the study only included subjects that albuminuria within the accepted normal range and not well established with regard to the association between body fat content and increased urinary albumin excretion. Therefore, the aim of our study was to comprehensively investigate the relationship of obesity measures with both low-grade albuminuria and increased

Conflict of interests: All of the authors have no relevant conflict of interests.

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urinary albumin excretion in community-based Chinese adults aged 40 years or older.

2. Methods

2.1. Population and study design

A cross-sectional study in a community was performed in Guangzhou, China, from June to November, 2011. The study population, design and protocols have been described previously (Ning, 2012; Bi et al., 2014). Study population is from the Risk Evaluation of cAncers in Chinese diabeTic Individuals: A lONgitudinal (REACTION) study, which has been set up as a multicenter prospective observational study aiming to evaluate the chronic diseases among Chinese population. REACTION study has been set up as a multicenter prospective observational study and was designed to evaluate the chronic diseases in Chinese population. A total of 10,104 participants aged 40 years or older were recruited and invited to participate by examination notice or home visits. In total, 9916 subjects had signed the consent form and agreed to participate in the survey, with a participation rate of 98.1%. Subjects who failed to provide information on urinary albumin and creatinine ($n = 160$) or body fat content ($n = 920$) or body mass index (BMI) ($n = 186$) or waist circumference ($n = 50$) were excluded from analysis. Finally, 8600 eligible individuals remained in the final analyses. The study protocol was approved by the Institutional Review Board of the Sun Yat-sen Memorial Hospital affiliated to Sun Yat-sen University. Written informed consent was obtained from each participant before data collection.

2.2. Clinical and biochemical measurements

A standard questionnaire was used and information on lifestyle factors, medical history, sociodemographic characteristics and family history was collected. Smoking or drinking habit was classified as 'never', 'current' (smoking or drinking regularly in the past 6 months) or 'ever' (cessation of smoking or drinking more than 6 months).

With the help of trained staff, all participants completed anthropometrical measurements according to standard protocols. Repeated blood pressure measurement was performed by the same observer three times with a 5 min interval. All the data obtained from an automated electronic device (OMRON, Omron Company, China). The average of three measurements of blood pressure was used for final analysis. Participants wore light indoor clothing without shoes, then body height and body weight were recorded to the nearest 0.1 cm and 0.1 kg. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Obesity was defined as BMI equal or greater than 28, and overweight was defined as BMI equal or greater than 24 and less than 28. Participants were in standing position and waist circumference was measured at the umbilical level at the end of gentle expiration. Body fat content was measured by using Omron Body Composition Monitor (Omron machine, BF-300, OMRON Corp., Kyoto, Japan), which is a hand-held bioelectrical impedance technique with bioelectrical impedance analysis to provide percentage of body fat. Compared with dual energy X-ray absorptiometry, bioelectrical impedance provides accurate results for assessment of body composition (Bosy-Westphal et al., 2008). A short form of the International Physical Activity Questionnaire (IPAQ) was used to estimate physical activity at leisure time by adding questions on frequency and duration of moderate or vigorous activities and walking. Separate metabolic equivalent hours per week (MET-h/week) were calculated for evaluation of total physical activity (Tomioka, Iwamoto, Saeki, & Okamoto, 2011).

Venous blood samples were collected for laboratory measurements. Fasting blood samples were collected to determine fasting plasma glucose (FPG), fasting serum insulin, serum lipids such as triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and creatinine was done using Beckman Biochemical autoanalyzer (Beckman CX-7 Biochemical Autoanalyser, Brea, CA, USA). High-performance liquid chromatography (Bio-Rad, Hercules, CA) was used to measure Hemoglobin A1c (HbA1c). Diabetes was diagnosed according to the 1999 World Health Organization diagnostic criteria. The abbreviated MDRD formula (Modification of Diet in Renal Disease formula) recalibrated for Chinese population was used to calculate estimated glomerular filtration rate (GFR) expressed in mL/min per 1.73 m^2 using a formula of eGFR $= 186 \times$ [serum creatinine $\times$ 0.011]$^{-1.154} \times$ [age]$^{-0.203} \times$ [0.742 if female] $\times$ 1.233 (De Leeuw et al., 2002). The insulin resistance index (homeostasis model assessment of insulin resistance, HOMA-IR) was calculated as fasting insulin (μIU/ml) $\times$ fasting glucose (mmol/L)/22.5 (Stehouwer et al., 2002).

2.3. Definition of low-grade albuminuria and increased urinary albumin excretion

The spot urine samples on the first morning were collected to measure the concentration of urine albumin and creatinine. Urine albumin was measured by chemiluminescence immunoassay (Siemens Immulite 2000, United States) and creatinine was measured by the Jaffe's kinetic method (Biobase-Crystal, Jinan, China) on the automatic analyzer, respectively. Increased ACR (calculated by dividing the urinary albumin concentrations by the urinary creatinine) was defined according to the ranges greater or equal than 30 mg/g. Low-grade albuminuria was defined according to the highest quartile of ACR in participants within the traditionally established normal range.

2.4. Statistical analysis

Statistical analysis was performed using SAS version 9.2 (SAS Institute Inc, Cary, NC, USA). For skewed variables, the data were presented as medians (interquartile ranges). Categorical variables were expressed as numbers or proportions. Continuous variables were presented as means $\pm$ standard deviation (SD). Comparisons between categorical variables were performed with the χ^2 test. Pearson's correlation and multivariate linear regression model were performed to evaluate the associations of obesity measure with ACR. Due to a non-normal distribution of ACR, body fat content, FPG, TG, and HOMA-IR, they were logarithmically transformed before statistical analysis. Smoking status and drinking status (non-current/current) were fitted as categorical variables. BMI (kg/m^2) was presented as quartiles: Quartile 1, < 21.49; Quartile 2, 21.49–23.42; Quartile 3, 23.43–25.53; and Quartile 4, ≥25.54; waist circumference (cm) was presented as quartiles: Quartile 1, <75; Quartile 2, 75–81.4; Quartile 3, 81.5–87.9; and Quartile 4, ≥88; body fat content(%) was presented as quartiles: Quartile 1, <25; Quartile 2, 25–29.6; Quartile 3, 29.7–33.5; and Quartile 4, ≥33.6.Linear regression analysis was used to test for trend across groups. Differences among groups were tested by one-way ANOVA and *post hoc* comparisons were performed by using Bonferroni correction.

The impact of obesity measures on the prevalence of low-grade albuminuria and increased urinary albumin excretion was analyzed. The logistic regression analysis (unadjusted and multivariate-adjusted) was used to assess the risk of prevalent low-grade albuminuria and increased urinary albumin excretion in relation to each quartile increase in BMI, waist circumference and body fat content levels. Model 1 was unadjusted. Model 2 was adjusted for age. Model 3 was further adjusted for sex, physical activity, FPG, TG, LDL-C and HbA1C. Model 4 was further adjusted for HOMA-IR. Model 5 was further adjusted for systolic blood pressure (SBP). Odds ratios (ORs) and the corresponding 95% confidence intervals (95% CIs) were