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Serum creatinine levels and risk of metabolic syndrome in a middle-aged and older Chinese population

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ABSTRACT

Background: The prevalence of metabolic syndrome (MetS) persistently increased. Several studies have found serum creatinine (SCr) concentrations related to cardiovascular disease and type 2 diabetes. The relationship between SCr concentrations and MetS is unknown.
Methods: We measured SCr concentrations and MetS in 22363 individuals (10,151 males, 12,212 females) from the Dongfeng-Tongji Cohort in Shiyan, China from 2008 to 2009.
Results: The prevalence of MetS was 30.6% in the study population. In the multivariable-adjusted logistic regression analyses, higher SCr concentrations were associated with a higher risk of MetS (P trend < 0.0001). Compared with the lowest extreme quintiles, subjects with the highest quintiles had 1.34 fold risk of MetS (95% confidence interval (CI): 1.22–1.47). The SCr concentrations were also associated with the individual component of MetS. In addition, higher SCr concentrations were associated with higher risk of MetS with more components.
Conclusions: There is a graded positive association between the SCr concentrations and MetS risk in a middle aged and older Chinese population. Higher SCr concentrations, even within normal ranges, were associated with higher risk of MetS. The SCr might be a useful indicator of MetS and its related diseases.

1. Introduction

Serum creatinine (SCr) concentration is used to assess renal function and is a commonly used indicator of chronic kidney disease (CKD) [1]. The concentration of SCr is influenced by multiple factors including age, gender, ethnic [2,3], diet, physical activity, muscle mass [4,5], medications [6–8], and renal conditions. Several cohort studies indicated that elevated SCr concentration was associated with increased risks of cardiovascular diseases (CVD) [9,10]. SCr was also found to be related to hypertension, obesity, and type 2 diabetes [6,11].

Metabolic syndrome (MetS), which refers to a cluster of factors (abdominal obesity, hypertension, dyslipidemia, and hyperglycemia) [12], could help to identify individuals at high risk of both CVD and type 2 diabetes [13,14]. In the United States, according to the revised National Cholesterol Education Program Adult Treatment Panel III (NCEPATPIII) definition, the age-adjusted prevalence of MetS was 34.2% [15]. In China, the overall age-standardized prevalence of MetS was 21.3% or 18.2% (based on the NCEPATPIII or the International Diabetes Federation criteria) [16]. The persistent increase of MetS becomes a serious public health concern because it raises the likelihood of increased prevalence of type 2 diabetes and CVD [15,17,18].

2. Materials and methods

2.1. Study population

We used the baseline information of Dongfeng-Tongji Cohort study and conducted a cross-sectional study. The Dongfeng-Tongji Cohort was launched in 2008, and conducted by Tongji Medical College, Huazhong University of Science and Technology and Dongfeng Motor Corporation (DMC). There are 27,009 (87% of 31,000) retirees of DMC who responded to a questionnaire and provided baseline blood samples. A detailed description of the study participants and

Abbreviations: DMC, Dongfeng Motor Corporation; MET, metabolic equivalent; MetS, metabolic syndrome; NCEPATPIII, National Cholesterol Education Program Adult Treatment Panel III.

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methods has been published elsewhere [19]. In this study, participants were excluded if they had missing data of SCr concentrations and/or one component of MetS. Those who had a history of cancer, urinary system diseases, thyroid disease or other severe diseases were also excluded. Based on the exclusion criteria, 2017 individuals without data on SCr concentrations and 1007 individuals without data on one or more component of MetS diagnostic criteria were excluded. In addition, 940 individuals with nephropathy or other urinary diseases, 407 with cancer, and 145 with thyroid disease or other severe diseases were excluded, as well as 103 individuals younger than 45 years old. Overall, 22,363 participants (10,151 males, 12,212 females) were included in the present study. The study was approved by the Medical Ethics Committee of the School of Public Health, Tongji Medical College, and Dongfeng General Hospital, DMC. All participants provided written informed consents.

2.2. Data collection

The epidemiological data were collected by a semi-structured questionnaire. The questionnaires included information on socio-demographic factors, health status, lifestyle, medical history and medication. Standing height, body weight, and waist circumference were measured with participants in light indoor clothing and without shoes. Blood samples were taken from all participants who fasted overnight. SCr, triglyceride, total cholesterol, lowdensity lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, and blood glucose concentrations were measured by the hospital's laboratory with Architect Ci8200 analyzer (Abbott Labs).

2.3. Assessment of SCr and covariates

SCr concentrations were categorized into 5 groups according to the quintiles of gender-specific distribution: <75, 75–83, 84–91, 92–101, and ≥102 μmol/l for males, and <62, 62–67, 68–73, 74–80, and ≥81 μmol/l for females, respectively. According to the respondents' self-reported information, education attainment was categorized as low (0 to 6 years), medium (7 to 9 y), and high (≥10 y); smoking status were grouped as current smokers, former smokers, and never smoked; drinking status were grouped as current drinkers, former drinkers, and never drinker. The amount of meat and seafood intake was assessed according to the following formula: frequency (times per week) × the amount of each time (g). Metabolic equivalent (MET) hours per week were calculated according to the following formula: MET coefficient of activity × duration (hours per time) × frequency (times per week). The meat intake, seafood intake, and MET were transformed into ordinal variables according to quartiles. We calculated estimated glomerular filtration rate (eGFR) by the Modification of Diet in Renal Disease (MDRD) equation based on the Chinese patients with chronic kidney disease (CKD) [20]; CKD was defined as eGFR < 60 ml/min per 1.73 m^2. Other variables were dichotomized as yes or no on the basis of the responses to questions on past history of hypertension, dyslipidemia, diabetes mellitus, coronary heart diseases (CHD), and the medication use of hypotensor, lipid lowering drugs, and diuretics.

2.4. Definition of the MetS

The MetS was defined by using the criteria recommended by the International Diabetes Foundation 2005 [21]. The definition includes central obesity (waist circumference ≥ 90 cm in Chinese men and ≥ 80 cm in Chinese women) plus any 2 of the following 4 factors: 1) high blood pressure: systolic ≥ 130 mm Hg, diastolic ≥ 85 mm Hg, or known treatment for hypertension; 2) hypertriglyceridemia: fasting serum triglycerides ≥ 1.7 mmol/l; 3) low HDL cholesterol: fasting HDL cholesterol < 1.0 mmol/l in men and < 1.3 mmol/l in women; and 4) hyperglycemia: fasting glucose concentration of ≥5.6 mmol/l (or ≥100 mg/dl) or known treatment for diabetes.

2.5. Data analysis

All statistical analyses were performed using SPSS 12.0 software (SPSS Inc.). Continuous variables were expressed as mean (SD) for normally distribution data or median (interquartile range) for skewed parameters. Analyses of variance were used to compare the means difference among 5 SCr quintile groups. Discrete variables were expressed as the percent values. We used χ^2 test to compare the proportion difference among 5 groups. We estimated the odds ratios (ORs) and 95% confidence intervals (CIs) for the different concentrations of SCr in MetS group compared to the non-MetS group based on univariate and multivariate logistic regression analysis. Multinomial logistic regression was used to estimate the ORs and CIs for different concentrations of SCr in different numbers of components of MetS group compared to the 0 components MetS group. The multivariable model was adjusted by age, gender, education, smoking, drinking, MET, meat and seafood intake, comorbidities, and medication use. We also used univariate general linear model to compare the concentrations of SCr in individuals without MetS and MetS with different components; the covariates were age, gender, smoking, education, and MET. *P*-values were tested for linear trend by treating the ordered categorical variable as a continuous variable. A 2-sided $P < 0.05$ was considered significant.

3. Results

3.1. Study group characteristics

The mean (SD) of concentration of SCr was 89.7 (26.4) μmol/l in males, 72.2 (15.8) μmol/l in females, and 80.1 (23.0) μmol/l in the whole population. The ranges of $P_{2.5}$ to $P_{97.5}$ in males and females were 58.0–131.0 μmol/l and 50.0–106.0 μmol/l, respectively. Exclusion of the individuals with CVD, hypertension, and diabetes in the present population (as the reference population), the gender-specific means (SD) for SCr concentrations were 86.9 (17.8) μmol/l in males, and 70.5 (13.6) μmol/l in females. The medians and 95% reference ranges ($P_{2.5}$ to $P_{97.5}$) in the reference population were 86 and 57 to125 μmol/l for males; 70 and 49 to 100 μmol/l for females. 4.2% of the whole population's SCr were higher than the upper limit of 95% reference range.

The prevalence of MetS was 23.0% in males, 36.9% in females, and 30.6% in the whole population. We categorized the whole population into 5 groups according to the gender-specific quintiles of SCr, the prevalence of MetS raised from 21.9% to 27.9% in males, 31.5% to 42.9% in females, and 27.1% to 36.3% in the whole population (Fig. 1).

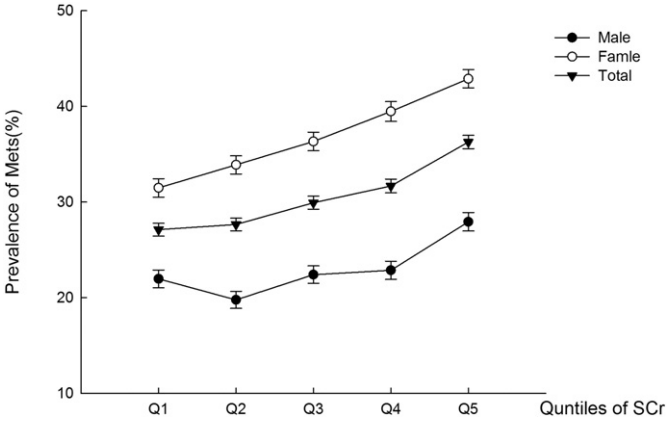

Fig. 1. Prevalence (95% CI) of the metabolic syndrome (MetS) by quintiles of serum creatinine (SCr) concentration among 22,363 participants. The quintiles of SCr concentration were calculated by gender respectively. In males, the cutoffs of SCr concentration were <75, 75–83, 84–91, 92–101, and ≥102 μmol/l; in females, the cutoffs were <62, 62–67, 68–73, 74–80, and ≥81 μmol/l.