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Insulin resistance is not independently associated with chronic kidney disease in Chinese population: A population-based cross-sectional study

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ABSTRACT

Background: Metabolic syndrome (MS) may modify the association of insulin resistance (IR) with chronic kidney disease (CKD), but the relevant studies were not enough. We evaluated whether IR is independently associated with CKD in Chinese population.
Methods: The data were from 2007–2008 China National Diabetes and Metabolic Disorders Study. CKD was defined as an estimated glomerular filtration rate <60 ml/min/1.73 m^2. IR was evaluated by using the homeostatic model assessment (HOMA-IR).
Results: A total of 11,143 individuals were included. Participants in the higher quartiles of HOMA-IR tended to have higher prevalence of CKD in general population ($P < 0.001$). However, there was no significant difference among the quartiles of HOMA-IR in population without MS ($P = 0.288$). In general population, the adjusted odds ratio of CKD was 1.183 (95% CI: 0.838–1.670), 1.543 (95% CI: 1.103–2.158), and 1.549 (95% CI: 1.079–2.223) in the second, third and fourth quartile of HOMA-IR relative to the lowest quartile, while the odds ratios in population without MS showed no significance in all higher quartiles.
Conclusions: IR was not an independently significant predictor of CKD in Chinese population, and MS may contribute greatly to the association between IR and CKD.

1. Introduction

China with a large population has a high prevalence of chronic kidney disease (CKD), which is estimated to be 10.8% and translated approximately a total of 119.5 million patients [1]. The increasing incidence of obesity, hypertension, and type 2 diabetes mellitus, coupled with aging population, will worsen the burden of CKD, which has substantial socioeconomic and public health consequence [2].

Insulin resistance (IR) is defined clinically in terms of the failure of insulin to maintain glucose homeostasis, which is indicated to be associated with CKD [3]. For example, end-stage renal disease is characterized by IR, and the severity of IR was is correlated with glomerular filtration rate (GFR) [4,5]. Meanwhile, IR is believed to play a central role in the pathogenesis of metabolic syndrome (MS), which is characterized as a cluster of metabolic abnormalities including obesity, hyperglycemia, hypertension and dyslipidemia [6,7]. IR and MS are not synonymous, despite there is significant overlap between the two terms. We previously reported that patients with MS had a 50% increase in the odds of CKD compared with individuals without MS [8]. Therefore, although several observational and prospective studies have indicated a relationship between IR and CKD in general or nondiabetic population [9–15], there were not enough studies concerning this relationship in populations without MS and these results were debatable [16,17]. It is of importance because MS may modify the association of IR with CKD, and the studies focusing the relationship between IR and CKD should better exclude patients with MS, rather than only exclude diabetic patients or adjust metabolic factors as variables.

Given the above background, we utilized the data of the 2007–2008 China National Diabetes and Metabolic Disorders Study, aiming to explore the association between IR and CKD in Chinese population, and to evaluate whether IR is independently associated with CKD in population without MS.

Abbreviations: CKD, chronic kidney disease; MS, metabolic syndrome; IR, insulin resistance; SCr, serum creatinine; HDL-c, high-density lipoprotein cholesterol; CNY, China Yuan; NECP-ATP-III, National Cholesterol Education Program Adult Treatment Panel III; MDRD, Modification of Diet in Renal Disease.

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2. Material and methods

2.1. Study population

The data in present study were from the 2007–08 China National Diabetes and Metabolic Disorders Study, which was a nationwide population-based cross-sectional survey and conducted between June 2007 and May 2008. The details of the study have been previously reported [8,18].

In brief, a multi-stage stratified sampling method was used to select a nationwide representative sample of Chinese adults with age above 20 years. A total of 17 study group field centers participated in the study, and 54,240 individuals from the general population were selected and invited. Of those individuals, 87.3% (47,325 individuals: 18,976 men and 28,349 women) participated, and 85.2% (46,239 individuals: 18,419 men and 27,820 women) completed the study. Since kidney function and insulin measurement were not the primary expected outcomes, serum creatinine (SCr) and fasting serum insulin were not measured at all of the centers. Therefore, only 11,143 individuals (4419 men and 6724 women) were included as study population, which had complete data on SCr, fasting serum insulin, fasting plasma glucose, systolic blood pressure, diastolic blood pressure, serum triglyceride level, serum high-density lipoprotein cholesterol (HDL-c), and waist circumference. The map of inclusive/exclusive centers can be seen in our previous report [8].

This study was approved by the institutional review boards or ethnics committees from all of the 17 participating centers. All the participants signed written informed consent prior to data collection. The 17 institutional review boards' approvals covered every participant in the study.

2.2. Data collection

A standard questionnaire was designed and administered by trained physicians or nurses at local health stations or in community clinics to collect information on demographic characteristics, lifestyle risk factors, and personal medical history. Educational level was categorized as college level or above, secondary school, and elementary school or below. Yearly family income was categorized as <10,000 China Yuan (CNY), 10,000–30,000 CNY and >30,000 CNY. Cigarette smoking was defined as a lifetime history of smoking at least 100 cigarettes. Frequency of drinking per week, favorite type of alcohol, and the amount of drinking per each occasion were recorded, and alcohol drinking was defined as the consumption of at least 30 g of alcohol per week for one year or more. Physical activity was defined as participating in moderate or vigorous activity for 30 min or more per day for at least 3 days a week.

Body weight and height were measured without shoes and in light clothing, and body mass index calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured at the middle point between the costal margin and iliac crest. Blood pressure was measured using a standardized mercury sphygmomanometer in the sitting position after at least 5 min of rest; 2 consecutive readings of blood pressure were taken on the same arm and the mean of the 2 measures was used for analysis.

Oral glucose tolerance test was performed on all subjects for the measurement of serum glucose and insulin. After at least 10 h of overnight fasting, participants with no history of diabetes were administered a standard 75 g glucose solution, while participants with a self-reported history of diabetes were given a steamed bun that contained approximately 80 g of complex carbohydrates for safety reasons. Fasting blood samples were also taken to measure serum triglyceride and HDL-c level. All laboratory measurements met a standardization and certification program [18].

IR was evaluated by using the homeostatic model assessment of insulin resistance (HOMA-IR) based on the following formula: fasting serum insulin (μU/ml) × fasting plasma glucose (mmol/l)/22.5 [19].

2.3. Definitions

Metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III criteria (NECP-ATP-III) as three or more of the following five metabolic components [6]: 1) elevated waist circumference: ≥90 cm (males) or ≥80 cm (females); 2) increased triglycerides: ≥1.69 mmol/l or the use of lipid medications; 3) elevated blood pressure: systolic blood pressure ≥130 mm Hg, or diastolic blood pressure ≥85 mm Hg, or the use of antihypertensive medications; 4) elevated fasting glucose: ≥5.6 mmol/l or the use of diabetes medications; 5) reduced HDL-c: <1.04 mmol/l (male) or <1.29 mmol/l (female).

The abbreviated equation developed by the Modification of Diet in Renal Disease (MDRD) study with modification for the Chinese population was used to calculate GFR [20]. Since most of our centers measured SCr on a Hitachi analyzer using the Jaffe's kinetic method, the following equation was adopted: $175 \times (\mathrm{SCr} \times 0.01131)\ (\mathrm{mmol/l})^{-1.234} \times \mathrm{age}\ (\mathrm{year})^{-0.179} \times (0.79 \text{ if female})$, which has been validated in the Chinese population and is also used by previous studies. CKD was defined as an estimated GFR <60 ml/min/1.73 m^2 according to the US National Kidney Foundation guidelines [21].

Diabetes was diagnosed based on Standard World Health Organization criteria [22]: fasting glucose ≥7.0 mmol/l or 2 h postprandial glucose ≥11.1 mmol/l, or self-reported use of diabetes medications.

Hypertension was defined according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [23]: systolic blood pressure of 140 mm Hg or greater, diastolic blood pressure of 90 mm Hg or greater, or self-reported use of antihypertensive medications.

2.4. Statistical analysis

Data were analyzed using SPSS 18.0 (SPSS Inc.). Data were expressed as the mean ± SD, median with interquartile range, or percentage as suitable. Comparisons between groups were analyzed by *t*-test or Mann–Whitney *U*-test for measurement data, and χ^2 test for enumeration data.

We used univariate and multivariate logistics analysis to determine odds ratios (ORs) for presence of CKD according to the quartiles of HOMA-IR (it was not normally distributed and thus Log transformed). The lowest quartile of HOMA-IR was used as reference. Odds ratios and 95% confidence intervals (95% CI) were calculated using a forward stepwise method. The covariables in the multivariate analysis were age, gender, ethnics, educational level, yearly family income, cigarette smoking, alcohol drinking, physical activities, waist circumference, fasting blood glucose, systolic blood pressure, diastolic blood pressure, serum triglyceride and high-density lipoprotein cholesterol. Data analyses were conducted firstly in general population to explore the association between IR and CKD, then in population without diabetes, population without hypertension, and population without MS to evaluate whether IR is independently associated with CKD. In addition, tertile analyses based on HOMA-IR were conducted as sensitivity analyses to test the robustness of the primary findings. A $P < 0.05$ was considered statistically significant.

3. Results

The characteristics of study population according to the quartiles of HOMA-IR were described in Table 1. A total of 11,143 participants were included as study population. The mean age was 46.2 years; 39.7% of participants were men and 98.9% were Han ethnics. The mean HOMA-IR was 1.76 ± 1.14, with range of 0.38–9.99. The overall proportion of diabetes, hypertension and MS was 9.4%, 29.8%, and 29.3%, separately. Participants who had higher quartile of HOMA-IR were more likely to have higher level of metabolic parameters (e.g., blood pressure, fasting glucose level, serum triglyceride level and