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The risk factors of mild decline in estimated glomerular filtration rate in a community-based population

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ABSTRACT

Objectives: The study aimed to analyze the relationship between metabolic variables and estimated glomerular filtration rate (eGFR) and explore the potential risk factors for a mildly reduced eGFR in a community-based population.

Design and methods: Cross-sectional study in 643 adults without a history of kidney disease whose eGFR levels were greater than 60 mL/min/1.73 m^2 according to the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI). Anthropometric measurements, blood pressure, fasting lipid profile and levels of fasting and post-load glucose, insulin, serum creatinine and uric acid (UA) were tested. The eGFR was calculated, and the correlations between eGFR and each variable were analyzed.

Results: The subjects were divided into two groups by using 90 mL/min/1.73 m^2 as the cut-off value of the eGFR. In the lower eGFR group, the age, systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), waist circumference (WC), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), 2 h post-load plasma glucose (2 h-PG) levels and UA were significantly increased, and the incidences of hypertension, diabetes, obesity, hypertriglyceridemia and hypercholesterolemia were also higher ($P<0.05$). A multiple linear stepwise regression analysis showed that the WC, SBP, FPG and UA were independently correlated with the eGFR after adjusting for the other covariables.

Conclusions: The WC, SBP, FPG and UA were closely related to the eGFR in the subjects whose eGFR levels were greater than 60 mL/min/1.73 m^2. The increased WC, SBP, FPG and UA may be the main risk factors for a mildly reduced eGFR.

Introduction

It is well known that chronic kidney disease (CKD), which is an important public health problem worldwide, has severely affected the quality of life of patients and has caused a heavy economic burden [1]. For instance, end-stage renal disease (ESRD), a serious consequence of CKD, has caused a high mortality rate of patients because many of them could not afford the expensive costs of dialysis and renal transplantation. In a longitudinal cohort study, the results showed that a mildly reduced GFR (<90 mL/min/1.73 m^2) predicted a 3-fold odds of progression to kidney disease [2]. Additionally, studies have displayed that except for the severe CKD or ESRD, the mild renal dysfunction also increased the risk of cardiovascular events such as arterial stiffness and even mortality [3,4]. Therefore, it suggests that screening risk factors for a mildly reduced renal function may be critical to prevent the pathological progression of CKD and its relevant complications.

The glomerular filtration rate (GFR) is commonly thought to be the important index for renal function assessment. However, an accurate and direct measurement of the GFR cannot be performed easily. Currently, the eGFR has served as an important and accessible index for estimating the GFR. According to the Modification of Diet in Renal Disease (MDRD) Study data, a series of equations for estimating the GFR was determined, and among of them, the simplified MDRD equation involving sex, age, creatinine level, and ethnicity has been widely applied to the eGFR [5]. Although the MDRD equations were based on the patients with CKD, studies found that the GFR level was underestimated by the equations, especially for mild renal insufficiency and in healthy population, which could lead to a misclassification of renal function [6]. Fortunately, a new equation for estimating the GFR was designed by the Chronic Kidney Disease Epidemiology

Abbreviations: BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, fasting serum triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FPG, fasting plasma glucose; 2 h-PG, 2 h post-load plasma glucose; FINS, fasting serum insulin; HOMA-IR, homeostatic model assessment of insulin resistance; Scr, serum creatinine; UA, uric acid; eGFR, estimated glomerular filtration rate.

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Collaboration (CKD-EPI), and studies showed that compared with the measured GFR using urinary or plasma clearance of exogenous filtration markers, the bias was significantly reduced in almost all subjects with different eGFR levels by using the CKD-EPI equation than the MDRD [7,8]. Consequently, we enrolled apparently healthy adults with normal eGFR and mildly reduced eGFR levels by adopting the CKD-EPI equation.

It is important to understand the risk factors of CKD; however, most previous studies focused on moderate to severe kidney disease that eGFR levels were less than 60 mL/min/1.73 m^2 [2,9–12], and few studies have been designed to discuss the risk factors for mild renal dysfunction. A recent study from China described the risk factors for mild renal dysfunction, but used the MDRD equation for assessing the GFR, and did not demonstrate the risk of other variables such as uric acid [13]. Here we used a different Chinese cohort and investigated the correlation between the eGFR and several previously unaddressed metabolic variables.

Methods

Subjects

All subjects were volunteers from the Luohuang community, recruited through a health status checkup in the urban area of Chongqing, which is a large city in southwestern China and more than 90% of residents participated in the study. The ages ranged from 20 to 76 years old. The exclusion criteria were the following: (1) subjects who had a history of kidney disease, including genetic, autoimmune or drug-induced kidney disease or another kidney dysfunction, such as nephritis, renal fibrosis or renal failure, or subjects who had a kidney transplant and were receiving dialysis treatment; (2) subjects who had secondary hypertension; (3) subjects who suffered from a malignant disease; (4) subjects who had gout; (5) subjects who smoked more than one cigarette per day, which lasted for at least one year; and (6) subjects who had an eGFR level less than 60 mL/min/1.73 m^2 by the CKD-EPI equation. Ultimately, 643 participants (464 males and 179 females) were enrolled in our study.

Informed consent was obtained from all participants before the survey, and this study was approved by the Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University.

Physical examinations

The heights and weights were measured in the fasting state. The waist circumference (WC) was measured at the midpoint between the lowest rib and the iliac crest [14]. The blood pressure was measured twice with a mercury sphygmomanometer using the left arm in the sitting position after resting for at least 5 minutes [15].

Laboratory assessments

Venous blood samples were collected between 07:00 and 09:00 following an overnight fast. The fasting serum lipid profile, including the total cholesterol (TC), fasting serum triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), was measured by an enzymatic assay (Wako Diagnostics, Tokyo, Japan). ApoA1 and ApoB were tested by nephelometry assays (Olympus Diagnostics, Tokyo, Japan). A standard 75-g oral glucose tolerance test (OGTT) was performed. The fasting plasma glucose (FPG) level was measured by a hexokinase assay (Olympus Diagnostics, Tokyo, Japan), and the fasting serum insulin (FINS) level was analyzed by a chemiluminescence assay (Roche Diagnostics, Mannheim, Germany). The serum creatinine (Scr) and uric acid (UA) levels were measured using enzymatic methods (Roche Diagnostics, Mannheim, Germany).

Parameter calculations

1. Body mass index (BMI) = weight (kg)/height^2 (m^2);
2. Homeostasis model of assessment for insulin resistance index (HOMA-IR) = FPG (mmol/L) × FINS (μU/mL)/22.5 [16];
3. GFR evaluation by the CKD-EPI equation [7]:

Sex	Scr (μmol/L)	eGFR [mL/min/1.73 m^2]
Females	≤62	$144\times(\mathrm{Scr}/62)^{-0.329}\times(0.993)^{\mathrm{age}}$
	>62	$144\times(\mathrm{Scr}/62)^{-1.209}\times(0.993)^{\mathrm{age}}$
Males	≤80	$141\times(\mathrm{Scr}/80)^{-0.411}\times(0.993)^{\mathrm{age}}$
	>80	$141\times(\mathrm{Scr}/80)^{-1.209}\times(0.993)^{\mathrm{age}}$

Statistical analysis

All statistical analyses were performed with SPSS (Statistical Product and Service Solutions) 11.0 (SPSS Inc, Chicago, IL, USA). Normally distributed data were presented as means ± SD. Data with a skewed distribution were presented as medians with the interquartile range and were log-transformed (based on 10) before parametric tests. An independent sample *t* test was used for comparisons of continuous variables, and chi-square test for categorical variables between two groups. A Pearson's correlation and multiple regression analysis were used to evaluate the associations between the eGFR and other variables. Statistical differences were defined by *P* values (two-tailed) less than 0.05.

Results

Clinical and biochemical characteristics

The basic characteristics of all subjects are displayed in Table 1. The study enrolled 643 participants, including 464 males and 179 females. The average level of eGFR was 101.87 ± 14.67 mL/min/1.73 m^2. 22.0% of the population had a mild eGFR decline (60 mL/min/1.73 m^2 ≤ eGFR

Table 1
Basic characteristics of the subjects.

Variable	Total cohort (n = 643)
Sex (males%)[a]	72.2%
Age (years)	42.7 ± 12.3
BMI (kg/m^2)	23.5 ± 3.1
WC (cm)	80.6 ± 10.1
SBP (mm Hg)	124.3 ± 16.1
DBP (mm Hg)	77.1 ± 10.3
TC (mmol/L)	4.74 ± 0.89
TG (mmol/L)[b]	1.19 (0.83–1.89)
HDL-C (mmol/L)	1.31 ± 0.35
LDL-C (mmol/L)	2.94 ± 0.78
ApoA1 (g/L)	1.46 ± 0.28
ApoB (g/L)	0.86 ± 0.20
FPG (mmol/L)	5.06 ± 0.80
2 h-PG (mmol/L)	7.00 ± 2.95
FINS (μU/mL)[b]	9.14 (6.02–13.01)
HOMA-IR[b]	2.04 (1.32–3.01)
Scr (μmol/L)	75.53 ± 13.83
UA (mmol/L)	0.31 ± 0.08
eGFR [mL/min (1.73 m^2)$^{-1}$]	101.87 ± 14.67

Abbreviations: BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, fasting serum triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; FPG, fasting plasma glucose; 2 h-PG, 2 h post-load plasma glucose; FINS, fasting serum insulin; HOMA-IR, homeostatic model assessment of insulin resistance; Scr, serum creatinine; UA, uric acid; eGFR, estimated glomerular filtration rate. Normal distribution of data was expressed as means ± SD.

[a] The categorical data was expressed by the percentage.

[b] Non-normal data was expressed as median with interquartile range and log-transformed before parametric tests.