

## Increased Risk of Chronic Kidney Diseases in Patients with Metabolic Syndrome: A 3-year Prospective Cohort Study\*

Ying HU<sup>1,2</sup>, Li-xin SHI<sup>#</sup>, Qiao ZHANG<sup>2</sup>, Nian-chun PENG<sup>2</sup>

<sup>1</sup>Department of Endocrine and Metabolic Diseases, the Second Affiliated Hospital of Soochow University, Soochow 215004, China

<sup>2</sup>Department of Endocrine and Metabolic Diseases, Affiliated Hospital of Guizhou Medical University, Guizhou 550004, China

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**Summary:** The relationship of metabolic syndrome (MS) and its components with incident chronic kidney disease (CKD) and rapid decline of estimated glomerular filtration rate (eGFR) was investigated. A total of 10 140 patients participating in the epidemiological study (Risk Evaluation of Cancers in Chinese Diabetic Individuals, REACTION) of risk factors of type 2 diabetes in China were followed up for 3 years, with MS being diagnosed by adult treatment panel III (ATP III) combined with waist circumference in Asian population and renal function being evaluated by  $eGFR < 60 \text{ mL} \cdot \text{min}^{-1} \cdot (1.73 \text{ m}^2)^{-1}$  and rapid decline of  $eGFR \leq 30\%$ . The results showed that as compared with the non-MS group, the adjusted odds ratios (ORs) of CKD and rapid decline of eGFR were 1.64 (OR: 1.64; 95% CI: 1.20–2.25,  $P < 0.05$ ) and 1.23 (OR: 1.23; 95% CI: 1.05–1.43,  $P < 0.05$ ) respectively in MS group. With the increase in the number (0, 1, 2, 3 and  $\geq 4$ ) of MS components, the prevalence of CKD was 1.42%, 1.44%, 2.80%, 3.42%, and 4.03% ( $P < 0.001$ ), respectively. The ORs of incident CKD were 1.67 (OR: 1.67; 95% CI: 1.22–2.27,  $P < 0.05$ ) for high TG, 1.50 (OR: 1.50; 95% CI: 1.10–2.05,  $P < 0.05$ ) for low HDL-C, and 1.39 (OR: 1.39; 95% CI: 1.02–1.91,  $P < 0.05$ ) for hyperglycemia. The risk for developing incident CKD was higher in the group with the highest HOMA-IR than in the group with the lowest HOMA-IR (OR: 1.83; 95% CI: 1.16–2.89,  $P < 0.05$ ). It is suggested that MS is an independent risk factor for incident CKD. The occurrence and development of CKD is closely related to insulin resistance.

**Key words:** metabolic syndrome; glomerular filtration rate; insulin resistance

Chronic kidney disease (CKD) has become one of the important diseases that seriously threaten human health, and its prevalence is increasing. Surveys by the National Health and Nutrition Examination Survey (NHANES) in 1988–1994 and in 2003–2004 showed that the prevalence of CKD increased from 10.0% to 13.1%<sup>[1]</sup>. The prevalence of estimated glomerular filtration rate (eGFR) [ $15\text{--}59 \text{ mL} \cdot \text{min}^{-1} \cdot (1.73 \text{ m}^2)^{-1}$ ] increased from 4.8% (in 1988–1994) to 6.9% (in 2011–2012)<sup>[2]</sup>. Recently, the prevalence of CKD in China was increasing and reached 10.8% in 2012<sup>[3]</sup>.

CKD and MS are both risk factors of all cause death and cardiovascular death<sup>[4–6]</sup>. In addition to gender, age, and ethnic factors, MS and its components, such as obesity, hypertension, diabetes, and lipid metabolism disorders, are independent risk factors for the development and progression of CKD<sup>[7, 8]</sup>. Nowadays, MS has become one of the most important risk factors of CKD. The total prevalence of MS in China reaches 24.5%, including 19.2% in males and 27.0% in females<sup>[9]</sup>. Our baseline data analysis had revealed a significant correlation of MS and its components with eGFR abnormalities. The abnormal risk of eGFR in the MS group was 1.75 times that of the non-MS group, and the risk of abnormal eGFR increased with the increase of MS components<sup>[10]</sup>. However, there have been few studies about the relationship between MS (including any of the components) and CKD in China, not to mention any prospective study. The causes of CKD may be related to chronic inflammation, oxidative stress, insulin resistance (IR), etc. IR is a central link in the pathophysiology of MS, but it's still

Ying HU, E-mail: 1040641282@qq.com

<sup>#</sup>Corresponding author, E-mail: slx1962@medmail.com.cn

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controversial whether IR is involved in the occurrence and development of CKD<sup>[8, 11]</sup>. We designed a large retrospective cohort to find the relationship between MS and CKD in Chinese. The aim of this study was to investigate the relationship of MS and its components with incident CKD and rapid decline of eGFR through a 3-year prospective follow-up study in 10 140 population older than 40 years old in our province.

## 1 MATERIALS AND METHODS

### 1.1 Study Populations and Design

A total of 10 140 baseline populations, aged from 40 to 79 years old, having lived in Zhaiji District of Guiyang for more than 10 years, and participating in the epidemiologic Study of Risk Evaluation of Cancers in Chinese Diabetic Individuals (REACTION, May to October 2011), were investigated from July to December of 2014 using the cluster random sampling method. The inclusion criteria were as follows: (1) baseline populations having lived in Zhaiji District of Guiyang for more than 10 years and participating in the REACTION; (2) the population participating in the REACTION and having obtained complete clinical information (ie, being included in the REACTION baseline database) was followed up (a total of 7993 people) for an average of 38 months (35–46 months). The exclusion criteria were as follows: (1) with kidney transplantation and dialysis; (2) with stroke and myocardial infarction; (3) with chronic nephritis, nephrotic syndrome, or renal cancer history; (4) baseline eGFR  $<60 \text{ mL}\cdot\text{min}^{-1}\cdot(1.73 \text{ m}^2)^{-1}$ ; (5) without complete data. After strict screening, 46 people with abnormal follow-up data were excluded; 30 people had no baseline data; 64 people had CKD; 1 person had nephrotic syndrome; 15 people had myocardial infarction; 104 people had baseline eGFR  $<60 \text{ mL}\cdot\text{min}^{-1}\cdot(1.73 \text{ m}^2)^{-1}$ ; 2 people had renal tumors; and 2647 people were lost. Finally, 7231 people were included (fig. 1). This study was conducted in accordance with the declaration of Helsinki. This study was approved by the Ethics Committee of Guizhou Medical University. Written informed consent was obtained from all participants.

### 1.2 Data Collection

All the enrolled residents were informed in advance to be fasting on the exact day of examination, namely being fasting for 8 to 10 h and having no calorie intake. A uniformly designed questionnaire was used, and specially trained medical professionals asked the detailed history of each person according to the questionnaire, including the name, gender, age, home address, ID number, contact phone number, nationality, education level, occupation, childbirth situation, medical insurance, and other general information so as to obtain the demographic characteristics, personal

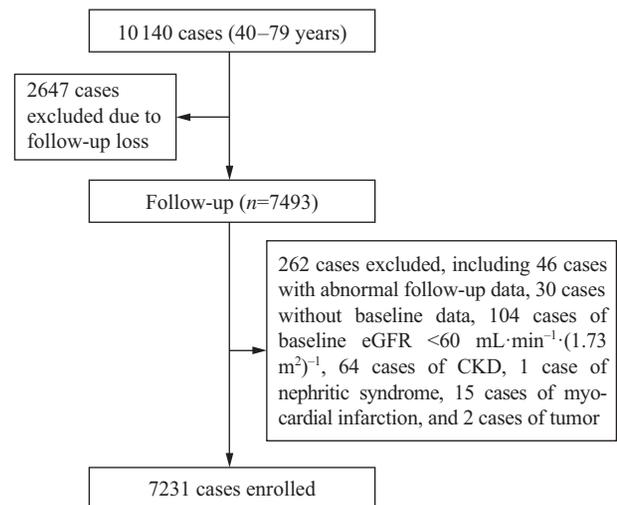


Fig. 1 Study population

and family medical history, and lifestyle risk factors, etc., as well as the history of diabetes, dyslipidemia, hypertension, cardiovascular events, cancer, or related treatments. Smoking was defined as smoking at least a cigarette per day for 6 months, drinking tea was defined as drinking at least one cup of tea per week for 6 months, and drinking was defined as drinking at least once a day for 6 consecutive months. The body height, weight, waist circumference, and blood pressure while wearing personal underclothes and taking off shoes were measured in each participant. The specific steps were as follows. For height, the participant took off shoes and hat, stood upright, backed up on the pillar, with the two heels being closer to each other while the toes being separated by 45°, and viewed the front flatly. Then, the head plate was pulled down and gently touched the top of the participant's head for the accurate reading (to 0.1 cm). For body weight, each participant wore only personal underclothes, took off shoes and hat, emptied the bladders and the stomach, and stood at the center of the weighing scale. The body weight was recorded when the pointer was stable (accurate to 0.1 kg). For blood pressure, each participant took a sitting position and the blood pressure was measured in the right upper limb, twice with an interval of 3–5 min. Each participant took a rest quietly for 10 min before measuring the blood pressure, avoiding force, emptying the bladder, stopping smoking 15 min before measurement, and avoiding drinking tea or coffee beverages before measurement. For waist circumference (WC), each participant only wore personal underclothes, unfastened the belt, stood vertically with two hands naturally drooping, two feet separating by 30–40 cm, and breathed calmly, and then the midpoint horizontal line of the anterior iliac crest with the lower edge of the 12th rib was measured. The tape shall be close to but not compress the skin (accurate to 0.1 cm). Body mass index (BMI) was

calculated by the formula: BMI=Body weight (kg)/Height (m<sup>2</sup>), and homeostatic model IR index (HOMA-IR) by: HOMA-IR=Fasting plasma glucose (mmol/L)×Insulin (mU/L)/22.5. The baseline population was also followed up in 2014 with the same content and methods as in 2011.

### 1.3 Laboratory Tests

All the non-diabetic persons were subjected to a 75 g anhydrous glucose tolerance test (OGTT), and the diabetic persons were given the 80 g cake test. The blood samples were collected and fasting plasma glucose (FBG) and 2-h postprandial plasma glucose (PBG) were tested on the same day. FBG was measured by an autocatalyst [Abbott Laboratories, Bio-Rad Multiqual (694, 696), USA] using the hexokinase method, and the fasting blood samples were firstly centrifuged and stored in EPP tubes at -70°C, and then delivered to Shanghai Ruijin Hospital in dry ice for testing triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) [Abbott Laboratories Bio-RadLipids Control (641, 642), USA], creatinine [Abbott Laboratories, Bio-Rad Quantitative Urine Control (376, 377), USA], and insulin [Abbott Laboratories, Dallas, Bio-Rad Lyphochek Immunoassay Plus Control Levels 1, 2, 3 (371, 372, 373), USA] by an automatic biochemical analyzer (ARCHITECT ci16200, Abbott Laboratories, USA) using the enzyme reagent method, phosphoglycerol phosphate oxidase method, accelerated selective dissolving reagent method, homogeneous enzyme assay, kinetic alkaline picric acid method, and chemiluminescent microparticle immunoassay, respectively. HbA1C was measured using high-performance liquid chromatography (HPLC) (Bio-Rad Laboratories, Inc., USA). All the kits were purchased from Shanghai Sangon Biotech Co., Ltd. (China).

### 1.4 Definition of Metabolic Syndrome

This study referred to the diagnostic criteria of NCEP-ATP III combined with the WC criteria in Asian population, as well as the diagnostic criteria in the references<sup>[12, 13]</sup>: any person meeting 3 or more items of the following 5 abnormalities can be diagnosed as MS: (1) SBP ≥130 mmHg and DBP ≥85 mmHg and/or taking antihypertensive drugs; (2) TG ≥1.69 mmol/L; (3) HDL-C <1.04 mmol/L in males and <1.30 mmol/L in females; (4) FPG ≥6.11 mmol/L; (5) WC ≥90 cm in males and ≥80 cm in females, or BMI ≥25 kg/m<sup>2</sup>.

### 1.5 Definition of Incident CKD and Rapid Decline of eGFR

The incident CKD was defined as eGFR <60 mL·min<sup>-1</sup>·(1.73 m<sup>2</sup>)<sup>-1</sup> during the follow-up period. Rapid decline of eGFR was defined as (final eGFR-initial eGFR)/(initial eGFR) × 100% ≤30%<sup>[14]</sup>.

### 1.6 Stratification Method

The follow-up people were divided into the

non-MS group and MS group. The patients with incident CKD in the eGFR-decline group were divided into the MS group and the non-MS group, and further subgrouped according to the number of MS components: group 0, without MS component; group 1, with one MS component; group 2, with 2 MS components; group 3, with 3 MS components; group 4, with 4 or 5 MS components. The HOMR-IR index of the participants was divided into group Q1-Q4 using the quartile method, namely group Q1, <1.41, group Q2, 1.41-2.02, group Q3, 2.02-2.86, and group Q4, >2.86.

### 1.7 Statistical Analysis

All the data were input into Excel and statistical analysis performed using SPSS 20.0 software. The measurement data were expressed as  $\bar{x} \pm s$ . The mean values between two groups were compared using the *t* test, and the comparison of mean values among multiple groups was made using one-factor ANOVA. The comparison of rate was done using the Chi-square test. The correlation was analyzed using the logistic regression analysis. Model 1 corrected the gender and age, and Model 2 further corrected the nationality, marital status, smoking, drinking, tea consumption, hypertension, and diabetic medication, with *P*<0.05 considered as statistical significance.

## 2 RESULTS

### 2.1 Comparison of Clinical Characteristics between Non-MS Group and MS Group

Totally, 7231 persons were enrolled in this study, including 1893 males (26.2%) and 5338 females (73.8%). During the 3-year follow-up period, CKD developed in 172 subjects (2.4%). The age, BMI, WC, blood pressure, FBG, TG, creatinine, HbA1C and HOMR-IR were significantly higher in the MS group than in the non-MS group (all *P*<0.05). The levels of HDL-C and eGFR were significantly lower in the MS group than in the non-MS group (both *P*<0.001, table 1).

### 2.2 Comparison of Risk of Incident CKD and Rapid Decline of eGFR between MS Group and Non-MS Group

After correcting the impact of age, gender, smoking, tea consumption, drinking, hypertension and diabetes-related drugs, the odds ratio (OR) of incident CKD in the MS group was 1.64 (OR: 1.64; 95% CI: 1.20-2.25, *P*<0.05), and the risk ratio of rapid decline of eGFR was 1.23 (OR: 1.23; 95% CI: 1.05-1.43, *P*<0.05). The ORs of incident CKD and rapid decline of eGFR in the MS group were significantly higher than those in the non-MS group (table 2).

### 2.3 Relationship of MS Components with Incident CKD

After correcting the impact of age, gender,

**Table 1 Baseline characteristics of participants according to presence of MS**

Parameters	Non-MS (n=5277)	MS (n=1954)	P value
Age (years)	57.3±7.8	59.1±7.6	<0.001
Male [n (%)]	1302 (24.7)	591 (30.2)	<0.001
BMI (kg/m <sup>2</sup> )	23.1±2.8	26.4±3.3	<0.001
Waist circumference (cm)	81.8±7.9	89.8±8.0	<0.001
SBP (mmHg)	117.3±16.3	132.4±18.8	<0.001
DBP (mmHg)	74.5±9.6	83.7±11.3	<0.001
FBG (mmol/L)	5.9±1.3	6.9±1.9	<0.001
HDL-C (mmol/L)	1.3±0.4	1.1±0.3	<0.001
LDL-C (mmol/L)	2.7±0.9	2.6±0.9	0.027
TC (mmol/L)	4.6±1.2	4.6±1.2	0.542
TG (mmol/L)	1.4±0.9	2.5±1.8	<0.001
Creatinine (μmol/L)	66.9±13.2	69.3±14.1	<0.001
HbA1C (%)	6.1±0.8	6.6±1.2	<0.001
eGFR [mL·min <sup>-1</sup> ·(1.73 m <sup>2</sup> ) <sup>-1</sup> ]	107.6±31.6	104.6±32.1	<0.001
HOMA-IR	2.0±1.9	3.4±2.9	<0.001
Smoker [n (%)] <sup>a</sup>	671 (12.7)	275 (14.1)	0.068
Tea drinker [n (%)] <sup>b</sup>	1813 (34.4)	778 (39.8)	<0.001
Alcoholic drinker [n (%)] <sup>c</sup>	445 (8.4)	160 (8.2)	0.390
Medication for hypertension [n (%)]	107 (2.0)	165 (8.4)	<0.001
Medication for diabetes [n (%)]	78 (1.5)	82 (4.3)	<0.001

P<0.05 between the non-MS group and the MS group.

<sup>a</sup>Smoker was defined as smoking at least one cigarette daily for at least 6 consecutive months; <sup>b</sup>Tea drinkers were defined as drinking at least one cup of tea per week in the precious 6 months; <sup>c</sup>Alcohol drinkers were defined as drinking wine ≥1 time(s) daily for at least 6 consecutive months.

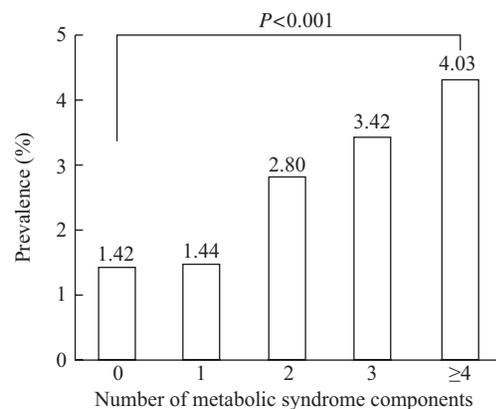
**Table 2 Odds ratios (ORs) (95% confidence interval) for incident CKD or/and rapid decline of eGFR<sup>a</sup> according to presence of MS at baseline**

	Incident CKD			Rapid decline of eGFR			CKD and rapid decline of eGFR		
	Non-MS	MS	P value	Non-MS	MS	P value	Non-MS	MS	P value
Incidence, n (%)	101 (1.91)	71 (3.63)		614 (11.6)	272 (13.9)		38 (0.72)	34 (1.74)	
Crude OR	1	1.93 (1.42–2.63)	<0.001	1	1.23 (1.05–1.43)	0.009	1	2.44 (1.53–3.89)	<0.001
Model 1	1	1.63 (1.19–2.24)	<0.001	1	1.21 (1.04–1.41)	0.015	1	2.06 (1.29–3.30)	0.002
Model 2	1	1.64 (1.20–2.25)	0.002	1	1.23 (1.05–1.43)	0.010	1	2.09 (1.30–3.35)	0.002

smoking, tea consumption, drinking, hypertension and diabetes-related drugs, the ORs for developing CKD in subjects with high TG, reduced HDL-C, and hyperglycemia were 1.67 (OR: 1.67; 95% CI: 1.22–2.27, P<0.05), 1.50 (OR: 1.50; 95% CI: 1.10–2.05, P<0.05), and 1.39 (OR: 1.39; 95% CI: 1.02–1.91, P<0.05), respectively (table 3). With the increase of the number of MS components (0, 1, 2, 3 and ≥4), the prevalence of CKD was also gradually increased, which was 1.42%, 1.44%, 2.80%, 3.42%, and 4.03%, respectively (fig. 2)

**2.4 Relationship of IR with Incident CKD and Rapid Decline of eGFR**

After correcting the impact of age, gender, smoking, tea consumption, drinking, hypertension and diabetes-related drugs, the comparison between the groups with the highest and lowest HOMA-IR index showed that the OR of incident CKD was 1.83 (OR: 1.83; 95% CI: 1.16–2.89, P=0.005), and the risk ratio of rapid decline of eGFR was 1.47 (OR: 1.47; 95% CI:



**Fig. 2** Prevalence of incident CKD by the number of components of MS

1.20–1.80, P<0.001) (table 4).

**3 DISCUSSION**

The baseline results in this study showed a

**Table 3 Odds ratios (ORs) (95% confidence interval) for incident CKD according to presence of each component for MS at baseline**

		Trait absent	Trait present	P value
High waist circumference	Incident CKD, <i>n</i> (%)	100 (2.1%)	72 (2.8%)	
	Crude OR	1	1.36 (1.00–1.85)	0.049
	Model 1	1	1.26 (0.92–1.72)	0.154
	Model 2	1	1.24 (0.91–1.71)	0.179
High blood pressure	Incident CKD, <i>n</i> (%)	126 (2.2%)	46 (3.2%)	
	Crude OR	1	1.47 (1.04–2.07)	0.027
	Model 1	1	1.26 (0.92–1.72)	0.154
	Model 2	1	1.24 (0.87–1.76)	0.237
High triglyceride	Incident CKD, <i>n</i> (%)	90 (2.0%)	82 (3.1%)	
	Crude OR	1	1.57 (1.16–2.13)	0.004
	Model 1	1	1.67 (1.22–2.28)	0.001
	Model 2	1	1.67 (1.22–2.27)	0.001
Reduced HDL cholesterol	Incident CKD, <i>n</i> (%)	75 (2.0%)	97 (2.7%)	
	Crude OR	1	1.36 (1.00–1.85)	0.048
	Model 1	1	1.50 (1.10–2.05)	0.011
	Model 2	1	1.50 (1.09–2.05)	0.013
High blood glucose	Incident CKD, <i>n</i> (%)	90 (1.8%)	82 (3.6%)	
	Crude OR	1	1.98 (1.46–2.6)	<0.001
	Model 1	1	1.39 (1.01–1.90)	0.039
	Model 2	1	1.39 (1.02–1.91)	0.038

**Table 4 Odds ratios (ORs) (95% confidence interval) for incident CKD or/and rapid decline of eGFR according to quartiles of HOMA-IR at baseline**

	HOMA-IR				P value
	Q1	Q2	Q3	Q4	
Range	<1.41	1.41–<2.02	2.02–2.86	>2.86	
CKD					
Crude OR	1	1.06 (0.64–1.76)	1.48 (0.93–2.36)	2.21 (1.43–3.42)	<0.001
Model 1	1	1.09 (0.65–1.81)	1.36 (0.85–2.20)	1.94 (1.24–3.03)	0.001
Model 2	1	1.11 (0.66–1.85)	1.33 (0.82–2.16)	1.83 (1.16–2.89)	0.005
Rapid decline of eGFR					
Crude OR	1	1.12 (0.91–1.39)	1.33 (1.08–1.63)	1.48 (1.21–1.81)	<0.001
Model 1	1	1.11 (0.90–1.38)	1.31 (1.07–1.61)	1.46 (1.19–1.78)	<0.001
Model 2	1	1.11 (0.90–1.38)	1.30 (1.06–1.61)	1.47 (1.20–1.80)	<0.001
CKD and rapid decline of eGFR					
Crude OR	1	1.13 (0.43–2.92)	2.90 (1.29–6.50)	4.05 (1.86–8.82)	<0.001
Model 1	1	1.13 (0.43–2.95)	2.66 (1.18–5.99)	3.51 (1.60–7.68)	<0.001
Model 2	1	1.19 (0.45–3.11)	2.62 (1.16–5.95)	3.06 (1.37–6.83)	0.001

significant correlation of MS and its components with the presence of CKD<sup>[10]</sup>. In this 3-year follow-up study, we found that MS was significantly associated with the development of CKD. Even after adjusting various influencing factors, the risk of incident CKD and rapid decline of eGFR was higher in the MS group than in the non-MS group. With the increase of the number of MS components, the risk of prevalent CKD also increased gradually, and the ORs of incident CKD and rapid decline of eGFR in the group with the highest HOMA-IR were higher than those in the group with the lowest HOMA-IR.

Recent studies have shown that MS is an important independent risk factor for CKD and microalbuminuria, and the risk of CKD among MS population is higher

than that in the non-MS population; meanwhile, MS is positively correlated with the decline of eGFR<sup>[7]</sup>. In follow-up studies in Korea<sup>[8]</sup>, Taiwan of China<sup>[15]</sup>, and Japan<sup>[16]</sup>, it has been found that MS is an independent risk factor leading to the occurrence and development of CKD. At present, there are few long-term follow-up studies targeting the relationship between MS and CKD in China. Therefore, we designed this prospective study targeting the impact of MS on CKD. The baseline results in this study showed that MS and its components were significantly associated with presence of CKD. As the MS components increased, the risk of presence of CKD increased<sup>[10]</sup>. During the follow-up period, we also found that MS was inversely associated with incident CKD and rapid decline of eGFR; among

the MS components, high TG, low HDL-C and hyperglycemia were independently associated with the occurrence and development of CKD. Contrary to this study, some studies suggested that elevated FBG levels or blood pressure were the strongest predictors of CKD in MS<sup>[8]</sup>. In this study, it was found that high TG was the most importantly independent risk factor of incident CKD, and the mechanism by which TG induces incident CKD and rapid progression of GFR may be related to lipid overload and lipotoxicity<sup>[17]</sup>.

IR is more and more considered to be an important factor in early kidney disease and does not depend on the occurrence of diabetes. IR may be an important link in MS-caused renal function decline<sup>[18]</sup>. In this study, the ORs of incident CKD and rapid decline of eGFR in the group with high HOMR-IR was significantly higher. It was speculated that IR may play a key role in the occurrence and development of renal dysfunction in MS population, and the mechanism may be that hyperinsulinemia increases oxidative stress, protein glycosylation oxidation, and lipid peroxidation, thus promoting the progression of renal insufficiency<sup>[19]</sup>. IR leads to glomerular and tubulointerstitial injury, and the core mechanism of such injury may be related to the inappropriate activation of the renin-angiotensin-aldosterone system<sup>[20]</sup>. One of the mechanisms of IR in chronic renal insufficiency found in mouse models revealed that it may be related to the alteration of key proteins in the Irf-PI3K-Akt pathway<sup>[21]</sup>. Therefore, IR can be an important therapeutic target for CKD patients.

This study was the first large-scale survey conducted in the southwest region using the cluster random sampling method. A total of 10 140 people aging 40–79 years old and having lived in Zhaiji District of Guiyang for more than 10 years were surveyed, so the data shift can be reduced. The above-mentioned baseline population participated in a 3-year follow-up study, and the follow-up rate was 73.9%. Secondly, OGTT (FBG, OGTT two-hour blood glucose and fasting insulin were measured simultaneously) was performed on all the study subjects, so it can more accurately diagnose diabetes and assess IR.

Our research has the following limitations. First, the study did not monitor urinary proteins, which will be added in subsequent studies. Second, there were more females in this study than males, so we corrected the impact of gender in the data. Third, the incident CKD and rapid decline of eGFR were only obtained through calculating the baseline and follow-up data at two time points, and more data at different time points can increase the accuracy of assessing incident CKD.

In conclusion, this 3-year prospective follow-up study showed a significant correlation of MS and its components with incident CKD, and the risk of incident CKD gradually increased with the increase of

the number of MS components. The rapid decline of eGFR may be the result of multiple risk factors in MS. Reducing IR can provide certain theoretical basis for the prevention and intervention of the occurrence and development of CKD, prompting that early monitoring and treatment of MS patients, as well as improving IR, is beneficial to our prevention and treatment of the occurrence and development of CKD.

#### Conflict of Interest Statement

The authors declare no conflict of interest.

#### REFERENCES

- 1 Coresh J, Selvin E, Stevens LA, *et al.* Prevalence of Chronic Kidney Disease in the United States. *JAMA*, 2007,298(17):2038-2047
- 2 Murphy D, McCulloch CE, Lin F, *et al.* Trends in Prevalence of Chronic Kidney Disease in the United States. *Ann Intern Med*, 2016,165(7):473-481
- 3 Zhang L, Wang F, Wang L, *et al.* Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet*, 2012,379(9818):815-822
- 4 Go AS, Chertow GM, Fan D, *et al.* Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*, 2004,351(13):1296-1305
- 5 Dilullo L, House A, Gorini A, *et al.* Chronic kidney disease and cardiovascular complications. *Heart Fail Rev*, 2015,20(3):259-272
- 6 Gurka MJ, Guo Y, Filipp SL, *et al.* Metabolic syndrome severity is significantly associated with future coronary heart disease in type 2 diabetes. *Cardiovasc Diabetol*, 2018,17(1):17
- 7 Hu W, Wu XJ, Ni YJ, *et al.* Metabolic syndrome is independently associated with a mildly reduced estimated glomerular filtration rate: a cross-sectional study. *BMC Nephrol*, 2017,18(1):192
- 8 Huh JH, Yadav D, Kim JS, *et al.* An association of metabolic syndrome and chronic kidney disease from a 10-year prospective cohort study. *Metabolism*, 2017,67(2):54-61
- 9 Li R, Li W, Lun Z, *et al.* Prevalence of metabolic syndrome in mainland China: a meta-analysis of published studies. *BMC Public Health*, 2016,16(1):296
- 10 Hu Y, Shi LX, Zhang Q, *et al.* Metabolic syndrome and its components associated with glomerular filtration rate in middleaged and elderly population. *Chin J Endocrinol Metab (Chinese)*, 2017,33(5):372-376
- 11 Li Y, Xie D, Qin X, *et al.* Metabolic syndrome, but not insulin resistance, is associated with an increased risk of renal function decline. *Clin Nutr*, 2015,34(2):269-275
- 12 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*, 2001,285(19):2486-2497
- 13 WHO Western Pacific Region, IASO IOTF. The Asia-Pacific Perspective: Redefining Obesity and Its Treatment. Sydney, Australia, Health Communications

- Australia Pty Limit Available: [http://www.wpro.who.int/nutrition/documents/Redefining\\_obesity/en/](http://www.wpro.who.int/nutrition/documents/Redefining_obesity/en/). Accessed 2014 May 4.
- 14 Coresh J, Turin TC, Matsushita K, *et al.* Decline in estimated glomerular filtration rate and subsequent risk of end-stage renal disease and mortality. *JAMA*, 2014,311(24):2518-2531
  - 15 Sun F, Tao Q, Zhan S. Metabolic syndrome and the development of chronic kidney disease among 118 924 non-diabetic Taiwanese in a retrospective cohort. *Nephrology*, 2010,15(1):84-92
  - 16 Hayashi K, Takayama M, Abe T, *et al.* Investigation of Metabolic Factors Associated with Incident CKD Over 1 Year in a Japanese Population without CKD. *Atheroscler Thromb*, 2017,24(8):863-875
  - 17 Lee HS. Mechanisms and consequences of hypertriglyceridemia and cellular lipid accumulation in chronic kidney disease and metabolic syndrome. *Histol Histopathol*, 2011,26(12):1599-1610
  - 18 Whaley-Connell A, Sowers JR. Insulin Resistance in Kidney Disease: Is There a Distinct Role Separate from That of Diabetes or Obesity? *Cardiorenal Med*, 2017,8(1):41-49
  - 19 Cooper SA, Whaley-Connell A, Habibi J, *et al.* Renin-angiotensin-aldosterone system and oxidative stress in cardiovascular insulin resistance. *Am J Physiol Heart Circ Physiol*, 2007,293(4):H2009-2023
  - 20 Nistala R, Whaley-Connell A. Resistance to insulin and kidney disease in the cardiorenal metabolic syndrome; role for angiotensin II. *Mol Cell Endocrinol*, 2013,378(1-2):53-58
  - 21 Wang Y, Wei RB, Yang Y, *et al.* Valsartan Alleviates Insulin Resistance in Skeletal Muscle of Chronic Renal Failure Rats. *Med Sci Monit*, 2018,24(4):2413-2419  
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