Letter to the Editor

Association of Metabolic Syndrome with Inflammation in Chinese Adults with Different Kidney Function*

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Chronic kidney disease (CKD) has become a worldwide public health problem, and currently, it affects approximately 10% of adults in the United States[1]. Meanwhile, it also has emerged as an important social challenge in China[2]. CKD has been reported to be a major risk factor for cardiovascular diseases, premature death, and end-stage renal disease[3]. Thus, it is necessary to determine the risk factors for CKD.

The metabolic syndrome (MS) is characterized by a group of metabolic risk factors to human, including abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance or glucose intolerance, and prothrombotic state, etc. Epidemiologic studies showed that insulin resistance and hypertension are major risk factors for the initiation and progression of CKD[4-5], and the MS is associated with an increased risk for proteinuria[6]. Therefore, MS is thought to be a risk factor for CKD. Furthermore, inflammation, increasingly prevalent in patients with CKD[7-8], has emerged as a major atherosclerotic risk factor in the past decade and has been associated with MS in the general population[9]. Results from the Third National Health and Nutrition Examination Survey (NHANES III) documented that MS and its component conditions are associated with inflammation in patients with varying levels of kidney function[10].

However, association of MS with inflammation has not been documented well in patients with moderate CKD, which is more important to the general population of the community. Accounting for the difference of genetic and environmental backgrounds between the Chinese population and Western countries, it is not clear whether these above associations were affected by racial discrepancies or not. Therefore, we examined the associations of MS and each of its component conditions with inflammation in patients with different levels of renal function. This might help to design future studies to target inflammation in the management of patients with moderate CKD.

All participants are provided informed consent and complete information. All experiments were performed in compliance with the Ethical Committee Approval and Good Laboratory Practices.

From January, 2007 to December, 2007, a total of 15 024 non-pregnant adults were enrolled in a community-based cross-sectional study in Chongqing, China. A total of 10 784 subjects, including 6759 males (age: 46.5±3.8 years) and 4025 females (age: 46.5±3.8 years) with complete information and then they were entered for the primary analysis. Subjects were given a standardized check-up, including a medical questionnaire, a physical examination, and a series of laboratory tests for a variety of adult diseases.

Of the total of 10 784 participants with complete set of data for all variables, 20.1% had MS and 14.6% had high CRP level. 36.8%, 38.3%, 34.5%, 6.3%, and 19.1% had HBP, HTG, AO, HFG levels, and low HDL-cholesterol levels, respectively. For renal function, 71.5%, 28.1%, and 0.4% (5 participants' eGFR: <30 mL/min/1.73 m^2 and 36 participants' eGFR: 30-60 mL/min/1.73 m^2) of the subjects had eGFR Level 3, Level 2, and Level 1, respectively. The prevalence of reduced kidney function was serious, indicating that it is important to investigate the association between MS and inflammation in chronic kidney disease.

From the highest to lowest eGFR group, MS was present in 18.6% (95% CI, 17.6-19.6), 24.4% (95% CI, 22.6-26.1), and 22.2% (95% CI, 6.5-37.9), whereas inflammation was present in 11.8% (95% CI, 10.1-13.7), 21.5% (95% CI, 17.9-25.5), and 60.0% (95% CI, 14.7-94.7), respectively.

Clinical characteristics including hsCRP, components of MS, myocardial infarction/stroke, cholesterol-lowering medication, but not age and smoking, showed statistical difference (P<0.05) between those with and without MS within each kidney function group (Table 1).

The present study demonstrated that a cross-sectional relationship of MS and its component conditions are associated with inflammation in Chinese with normal and mild reduced kidney function. This is similar to the results reported previously[10].

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Table 1. Clinical Characteristics of Participants with and without MS at Varying Levels of Kidney Function

Parameters	eGFR (mL/min)					
	≥90		60-89		<60	
	MS Present (*n*=1155; 18.6 %)	MS Absent (*n*=5055; 81.4%)	MS Present (*n*=550; 24.3%)	MS Absent (*n*=1709; 75.7%)	MS Present (*n*=21; 77.8%)	MS Absent (*n*=6; 22.2%)
eGFR (mL/min)	110.4 (109.5-111.3)	111.0 (110.6-111.5)	79.8 (79.2-80.4)	81.0 (80.6-81.3)	55.7 (51.0-60.5)	49.3 (42.2-56.5)
hsCRP (mg/L)[a,b,c]	1.7 (1.4-1.9)	1.1 (0.9-1.2)	2.1 (1.6-2.6)	1.4 (1.2-1.7)	2.9 (1.6-4.7)	2.0 (1.0-3.2)
Demographics						
Age (y)	46.4±3.7	46.2±3.7	46.9±3.6	47.0±3.9	48.3±4.5	48.4±4.3
Male (%)[a,b,c]	81.1 (78.9-83.4)	52.5 (51.2-53.9)	91.3 (88.9-93.6)	71.4 (69.6-73.9)	100 (54-100)	57.1 (35.9-78.3)
Components of MS						
High fasting Glucose (%)[a,b,c]	22.3 (19.9-24.7)	1.9 (1.5-2.2)	21.1 (17.8-24.5)	1.9 (1.2-2.5)	33.3 (4.3-77.7)	4.8 (0.1-23.8)
High blood Pressure (%)[a,b,c]	80.4 (78.1-82.7)	24.2 (23.0-25.4)	76.2 (72.6-79.8)	30.1 (28.0-32.3)	83.3 (35.9-99.6)	28.6 (9.3-47.9)
Abdominal obesity (%)[a,b,c]	87.3 (85.4-89.2)	20.0 (18.9-21.1)	87.8 (85.1-90.6)	26.9 (24.8-29.0)	100.0 (45.9-100.0)	33.3 (13.2-53.5)
Low HDL-C (%)[a,b,c]	53.0 (50.1-55.9)	10.1 (9.2-10.9)	60.0 (55.9-64.1)	9.8 (8.4-11.2)	33.3 (4.3-77.7)	14.3 (4.1-36.3)
High triglycerides (%)[a,b,c]	92.6 (91.0-94.1)	24.3 (23.1-25.4)	92.4 (80.9-94.4)	27.0 (24.9-29.1)	66.7 (22.3-95.7)	47.6 (25.7-70.2)
Other clinical characteristics						
Myocardial infarction/stroke (%)[a,b,c]	6.3 (3.2-8.6)	1.2 (0.6-1.7)	15.4 (10.2-17.5)	3.7 (2.5-4.9)	20.6 (12.4-32.5)	17.4 (15.3-19.1)
Smoking (%)	26.5 (24.7-28.9)	31.3 (28.2-34.3)	28.7 (26.3-29.7)	32.6 (30.5-34.8)	19.0 (12.0-27.0)	14.5 (8.9-20.2)
Cholesterol-lowering medication (%)[a,b,c]	4.4 (3.1-4.9)	0.9 (0.2-1.9)	12.4 (8.4-14.2)	2.1 (1.3-4.5)	18.9 (12.1-27.3)	3.9 (1.7-8.9)

Note. Values expressed as mean (95% CI) or percent (95% CI). To convert creatinine clearance from mL/min to mL/s, multiply by 0.01667; HDL cholesterol (HDL-C) from mg/dL to mmol/L, multiply by 0.02586; triglycerides from mg/dL to mmol/L, multiply by 0.01129. [a]$P<0.05$ comparing MS with absence of MS in patients with eGFR of 90 mL/min or greater. [b]$P<0.05$ comparing MS with absence of MS in patients with eGFR of 60 to less than 90 mL/min. [c]$P<0.05$ comparing MS with absence of MS in patients with eGFR less than 60 mL/min.

Association of MS with Inflammation In multiple logistic regression models, MS was associated with inflammation in people at Level 3 and Level 2 eGFR (Table 2) ($P<0.05$), but not at Level 1 ($P>0.05$). After adjustment by age, sex, history of smoking, history of myocardial infarction or stroke and cholesterol-lowering medications, MS was associated with inflammation in people at Level 3, not at Level 1 and Level 2 eGFR ($P>0.05$). These data revealed that compared with patients without MS, the odds of inflammation for patients with MS was higher in patients with normal kidney function regardless of adjustment for other conditions.

Associations of Number of Component Conditions of MS with Inflammation There were associations of inflammation with component conditions number 2 to 4 of MS at Level 3, and there were associations of inflammation with 2 and 3 number of component conditions of MS at Level 2 eGFR, (Table 2). Our study indicated that traditional atherosclerotic risk factors, such as components of MS, and nontraditional atherosclerotic risk factors, such as inflammation, might be interlinked in CKD status. Thus, traditional and nontraditional atherosclerotic factors might play a synergistic role in the development of atherosclerosis in patients with CKD.

Associations of Each Component Condition of MS with Inflammation In Model A (multivariate logistic regression model adjusted by demographics, smoking, history of myocardial infarction or stroke, and the use of cholesterol-lowering medications) (Table 3). HFG, HBP, AO, and HTG levels were significantly associated with inflammation at Level 3 eGFR; HBP, AO, and HTG levels were significantly associated with inflammation at Level 2 eGFR. In Model B (multivariate logistic regression model adjusted by all 5 components of MS, demographics, smoking, history of myocardial infarction or stroke,

and the use of cholesterol-lowering medications) (Table 3), HFG and AO were significantly associated with inflammation at Level 3 eGFR; only HBP was significantly associated with inflammation at Level 2 eGFR. Further study is needed to determine if racial differences are implicated in the underlying biological mechanism.

MS, metabolic syndrome. '-' No. Odds Ratio (95% CI) of the presence of infammation parameters estimated for the CRP Level that not met the 0.05 significance level for entering into the mable.

Limitations Although the relationship of MS and some of its component conditions are associated with inflammation in Chinese with reduced kidney function, there is still a limitation of this study due to its cross-sectional design. Therefore, further study is recommended to confirm this point.

In a conclusion, our study investigated the associations of MS and its component conditions with inflammation in Chinese with different renal function levels. We revealed that there were an association of MS and some of it components with inflammation at normal and mildly reduced kidney function. It might be an evidence for concluding the development of the disease. Further study is needed to confirm the present findings.

Table 2. Associations of MS with Inflammation at Different Levels of Kidney Function in Logistic Regression Models

Items	Variance	eGFR (mL/min)		
		≥90 (*n*=7713)	60-89 (*n*=3030)	<60 (*n*=41)
MS with Inflammation	Unadjusted	1.87 (1.37-2.56)	1.67 (0.98-2.84)	>10 000 (OR<0.001 and OR>10 000)
	Adjusted for other conditions[a]	1.97 (1.31-2.96)	-	-
No. of component conditions	0	Reference	Reference	Reference
	1	-	-	-
	2	2.63 (1.44-4.84)	2.74 (1.22-6.16)	-
	3	3.92 (1.94-7.90)	2.79 (1.05-7.42)	-
	4	4.07 (1.74-3.52)	-	-
	5	-	-	-

Note. Values expressed as odds ratio (95% CI) of the presence of inflammation, defined as CRP level greater than 3 mg/L. Each column represents a model adjusted for age, sex, race, smoking, history of myocardial infarction or stroke and use of cholesterol-lowering medications. To convert estimated glomerular filtration rate in mL/min to mL/s, multiply by 0.01667. [a]Other conditions include age, sex, history of smoking, history of myocardial infarction or stroke and cholesterol-lowering medications. '-'No Odds Ratio (95% CI) of the presence of inflammation parameters estimated for the CRP level that not met the 0.05 significance level for entering into the model.

Table 3. Associations of Each Component Condition of Metabolic Syndrome with Inflammation at Different Levels of Kidney Function in Logistic Regression Models

Component of MS	eGFR (mL/min)					
	≥90 (*n*=7713)		60-89 (*n*=3030)		<60 (*n*=41)	
	Model A[*]	Model B[†]	Model A[*]	Model B[†]	Model A[*]	Model B[†]
High fasting glucose	2.18 (1.24-3.81)	1.86 (1.03-3.36)	-	-	-	-
High blood pressure	1.55 (1.06-2.26)	-	1.63 (1.02-2.73)	1.68 (1.02-2.78)	-	-
Hypertriglyceridemia	1.66 (1.15-2.39)	-	1.78 (1.11-2.86)	-	-	-
Abdominal obesity	2.00 (1.36-2.96)	1.71 (1.13-2.57)	1.74 (1.05-2.88)	-	-	-
Low HDL cholesterol	-	-	-	-	-	-

Note. Values expressed as odds ratio (95% CI) of inflammation, defined as CRP level greater than 3 mg/L. Each cell represents a separate model. To convert estimated glomerular filtration rate in mL/min to mL/s, multiply by 0.01667. [*]Adjusted for age, sex, smoking, history of myocardial infarction or stroke, exercise level, and cholesterol-lowering medications. [†]Adjusted for other component conditions of metabolic syndrome, age, sex, smoking, history of myocardial infarction or stroke and cholesterol-lowering medications.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing financial interests.

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