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ORIGINAL RESEARCH

Metabolic Syndrome Is Associated With Rapid Estimated Glomerular Filtration Rate Decline In A Chinese Community-Based Population

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Purpose: This study aimed to determine the relationship between the metabolic syndrome (MetS) and rapid estimated glomerular filtration rate (eGFR) decline in a Chinese commu-

Patients and methods: A total of 3108 participants were recruited between December

2011 and July 2014 from an observational study cohort designed for the study of

atherosclerotic diseases in Beijing, China. The outcome was a rapid eGFR decline.

Subgroup and interaction analyses were performed with respect to a number of

Results: Over a median follow-up period of 2.34 (IQR: 2.29-2.41) years, the overall

incidence of rapid eGFR decline was 7.24%. We found that the MetS was significantly

associated with the risk of rapid eGFR decline (odds ratio [OR]=1.69, 95% confidence

interval [CI]: 1.28–2.23, p<0.001) in a model adjusted for age, sex, and eGFR, and this

relationship remained significant after adjustment for smoking, drinking, and lowdensity lipoprotein-cholesterol (OR=1.78, 95% CI: 1.34-2.35, p<0.001). Waist circumference (OR=1.38, 95% CI: 1.04-1.83, p=0.027), triglycerides (OR=1.40, 95% CI: 1.05-1.86, p=0.022), blood pressure (OR=2.05, 95% CI: 1.49-2.82, p<0.001), and fasting plasma glucose (OR=2.12, 95% CI: 1.57-2.85, p<0.001), but not high-density lipoprotein-cholesterol (OR=1.26, 95% CI: 0.94-1.69, p=0.117), were positively associated with the risk of rapid eGFR decline. Similarly, an increase in the number of MetS components present was associated with an increase in the risk of rapid eGFR decline. Furthermore, this association was modified by smoking status (OR=3.78, 95%

Conclusion: The MetS independently predicted rapid eGFR decline in a Chinese community-based cohort recruited for the study of atherosclerosis. The relationship between the MetS and the risk of rapid eGFR decline was modified by smoking status. Keywords: metabolic abnormalities, estimated glomerular filtration rate, kidney function,

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Plain Language Summary

CI: 1.68-8.49, p-interaction=0.030).

atherosclerosis

Why Was The Study Done?

- Metabolic syndrome (MetS) has been considered as a serious public health problem globally. MetS shares many risk factors with chronic kidney disease (CKD).
- Few data exist regarding the predicting value of MetS for rapid eGFR decline in Chinese community-based populations.

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What Did The Researchers Do And Find?

- In this Chinese community-based cohort, MetS was significantly associated with the risk of rapid eGFR decline.
- Of individual components of MetS, waist circumference, triglycerides, blood pressure, and fasting plasma glucose except HDL-C were all associated with the risk of rapid eGFR decline. High fasting plasma glucose and blood pressure were the two most important risk factors.
- The risk of rapid eGFR decline increased with an increase in the number of MetS components.
- The MetS-rapid eGFR decline association was modified by the status of current smoking.

What Do These Results Mean?

• The prospective intervention and treatment of MetS components may help slowdown the decline in kidney function and confer potential benefits.

Introduction

The metabolic syndrome (MetS) is a cluster of risk factors for cardiovascular disease, consisting of abdominal obesity, dyslipidemia (high triglyceride and low high-density lipoprotein-cholesterol [HDL-C] concentrations), high blood pressure (BP), and high fasting glucose or diabetes and is considered to be a serious public health problem globally. In US adults, the prevalence of the MetS was 18.3% among those aged 20–39 years and 46.7% among those aged ≥ 60 years.¹ In mainland China, the prevalence of the MetS has been reported to be 24.5% in people aged ≥ 15 years and to increase with age.²

Chronic kidney disease (CKD), another risk factor for cardiovascular disease, is an important public health problem and is highly prevalent (10.8%, 95% CI: 10.2-11.3%) in China.⁶ The MetS shares many risk factors with CKD. Indeed, previous studies have shown that the MetS is a risk factor for type 2 diabetes mellitus, cardiovascular disease, and all-cause mortality.3-5,24 Notably, there is a significant association between the MetS and CKD.^{7,10,17–19} Patients with the MetS have a 2.5-fold higher risk of CKD.⁸ In addition, a cohort study conducted in Japan suggested that the MetS is associated with the progression of CKD,¹¹ and a 10-year prospective cohort study showed that individuals with the MetS have a higher risk of rapid estimated glomerular filtration rate (eGFR) decline than those without (OR: 1.20, 95% CI: 1.04–1.39).¹² However, the relationship between the MetS and rapid eGFR decline, especially in Chinese people who do not have CKD or cardiovascular disease, is not well understood. Given that prospective cohort studies have not been conducted to address this question in mainland China, we aimed to determine the relationship between the MetS and rapid eGFR decline in a Chinese population.

Materials And Methods Study Population

Participants were recruited from among the participants in an observational cohort survey regarding atherosclerosis diseases that was conducted between December 2011 and July 2014 in Beijing, China. The study procedures have been documented elsewhere.²¹ Initially, 5962 participants aged \geq 40 years who had undergone a baseline survey were invited to participate in a follow-up examination in 2014, of whom 3823 (64.1%) responded on site. From these, participants who were missing blood creatinine values at revisit were excluded (n=14). Then, participants with coronary heart disease, stroke, peripheral arterial disease (ABI<0.9), or CKD, defined by an eGFR of <60 mL/min/1.73 m², at baseline were excluded (n=701). Thus, 3108 participants were eligible for the present study.

This study was approved by the Ethics Committee of Peking University First Hospital. Written informed consent was obtained from all the participants before data collection.

Measurements Made

As described previously,²¹ baseline data were collected by trained researchers according to standard operating procedures. All the participants were interviewed using a standardized questionnaire that included questions about demography, health behavior, and medical history. Current smoking was defined as smoking at least one cigarette per day for at least 6 months and current drinking was defined as drinking alcohol at least once per week for at least 6 months.

The participants underwent a series of anthropometric and other measurements. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. The participants were required to rest for 5 mins before seated brachial blood pressure measurements were performed. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the right arm using a calibrated Omron HEM-7117 electronic sphygmomanometer. Triplicate measurements were performed with 1 min between successive readings, and the mean value was calculated and used in the analysis.

Venous blood samples were obtained from the forearm of participants that had fasted overnight. Serum or plasma samples were separated within 30 mins and stored at -80° C. Fasting blood glucose (FBG), 2-hr glucose concentration in the standard 75-g oral glucose tolerance test (OGTT), HDL-C, low-density lipoprotein (LDL)-cholesterol, and triglyceride (TG) concentrations were measured using a Roche C8000 Automatic Analyzer. Serum creatinine concentration at baseline and follow-up were analyzed using the enzymatic method and Jaffe's kinetic method, respectively, as described previously.²¹ The values obtained were transformed using the enzymatic equation and standardized to one core laboratory values. EGFR was calculated using the equation published by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).²²

Definition Of The Metabolic Syndrome

The criteria for the MetS²⁵ were those developed by the National Heart, Lung and Blood Institute/American Heart Association and International Diabetes Federation. We defined the MetS as the presence of any three of the following five components: (1) central adiposity, based on ethnicity-specific waist circumference cut-offs (\geq 90 cm in men or \geq 80 cm in women); (2) triglyceride (TG) \geq 1.7 mmol/L or the use of antihyperlipidemic therapy; (3) HDL cholesterol < 1.0 mmol/L in men or <1.3 mmol/L in women or the use of antihyperlipidemic therapy; (4) SBP \geq 130 mm Hg or DBP \geq 85 mm Hg or the use of antihypertensive medication; (5) FBG \geq 5.6 mmol/L or a diagnosis of diabetes.

Outcomes

The study outcome was rapid eGFR decline, which was defined as a decline in eGFR of >3 mL/min/1.73 m²/year.²³

Statistical Analysis

Hypertension was self-reported, or defined by an SBP \geq 140 mmHg or a DBP \geq 90 mmHg, or the use of antihypertensive therapy. Diabetes mellitus was self-reported, or defined by the presence of an FBG of \geq 7.0 mmol/L or a 2-hr OGTT value of \geq 11.1 mmol/L, or the use of antidiabetic therapy. Dyslipidemia was self-reported, or defined by a TG concentration \geq 1.70 mmol/L, a total cholesterol (TC) concentration \geq 5.18 mmol/L, an LDL-C concentration \geq 3.37 mmol/L, an HDL-C concentration <1.04 mmol/L, or the use of antihyperlipidemic therapy.

Data are presented as the mean \pm standard deviation (SD) or as numbers and percentages for continuous or categorical variables, respectively. The MetS and rapid eGFR decline were analyzed as dichotomous variables, and BMI was analyzed as both a continuous and a categorical variable. The characteristics of all the participants and the differences among the participants, according to the presence or absence of the MetS were compared using Student's t-test for normally distributed continuous variables or Pearson's χ^2 test for categorical variables. Univariate and multivariate logistic regression models were used to characterize the relationship between the MetS and rapid eGFR decline. The covariates adjusted for in the multivariate analysis were sex, age, baseline eGFR, LDL-C concentration, current smoking, and current drinking. Subgroup and interaction analyses were performed with regard to all these covariates. P < 0.05(two-sided) was considered to represent statistical significance. Data analysis was performed using Empower(R) (www.empowerstats.com, X&Y solutions, Inc. Boston MA) and R (http://www.R-project.org).

Results

Table 1 shows the baseline characteristics of the participants, both overall and categorized according to the presence or absence of the MetS. Thirty-five percent of the participants were men, and they had a mean age of 55.78 \pm 8.09 years and a mean BMI of 25.95 \pm 3.34 kg/ m². Forty-four-point-eight percent had hypertension, 14.90% had diabetes mellitus, and 41.57% had the MetS. Their mean baseline eGFR was 101.89 ± 10.25 mL/min/1.73 m². Participants with the MetS, of whom 66.60% were women, were older, had a higher BMI, had higher prevalence of hypertension, diabetes mellitus, and renal function decline, but had a lower eGFR at baseline. Furthermore, participants with the MetS had a significantly higher waist circumference, SBP and DBP, higher TG, TC, and LDL-C concentrations, and a lower HDL-C concentration.

Over a median follow-up period of 2.34 years (25th– 75th centile: 2.29–2.41), the incidence of rapid eGFR decline was 7.24%, and 121 (9.37%) of the participants with the MetS and 104 (5.73%) without demonstrated a rapid decline in eGFR.

Table 2 shows the effects of the MetS on the incidence of rapid eGFR decline, determined using multivariate regression analysis. A positive association between the MetS and rapid eGFR decline was obtained after

| Table I | Baseline | Characteristics | Of The | Participants |
|---------|----------|-----------------|--------|--------------|
|---------|----------|-----------------|--------|--------------|

| Variables | Overall | Without MetS | With MetS | P-value |
|--------------------------------------|-----------------|-----------------|-----------------|---------|
| N, n (%) | 3108 | 1816(58.43) | 1292(41.57) | |
| Age, years | 55.78 ± 8.09 | 54.66 ± 7.84 | 57.36 ± 8.17 | <0.001 |
| Male, n (%) | 1087 (35.00) | 656 (36.10) | 431 (33.40) | 0.111 |
| Waist circumference, cm | 82.47 ± 8.45 | 79.32 ± 7.74 | 86.91 ± 7.35 | <0.001 |
| BMI, kg/m ² | 25.95 ± 3.34 | 24.78 ± 2.99 | 27.61 ± 3.08 | <0.001 |
| SBPm, mmHg | 132.62 ± 16.18 | 128.15 ± 15.31 | 138.90 ± 15.26 | <0.001 |
| DBPm, mmHg | 75.32 ± 9.61 | 73.55 ± 9.05 | 77.80 ± 9.82 | <0.001 |
| Triglycerides ^ª , mmol/L | 1.29(0.91-1.86) | 1.06(0.79–1.41) | 1.81(1.29-2.45) | <0.001 |
| Total cholesterol, mmol/L | 5.35 ± 0.99 | 5.27 ± 0.92 | 5.44 ± 1.07 | <0.001 |
| HDL-C, mmol/L | 1.45 ± 0.38 | 1.57 ± 0.37 | 1.27 ± 0.32 | <0.001 |
| LDL-C, mmol/L | 3.26 ± 0.83 | 3.19 ± 0.78 | 3.37 ± 0.89 | <0.001 |
| eGFR, mL/min per 1.73 m ² | 101.89 ± 10.25 | 102.77 ± 10.00 | 100.66 ± 10.48 | <0.001 |
| Current smoking, n (%) | 594 (19.10) | 357 (19.70) | 237 (18.30) | 0.358 |
| Current drinking, n (%) | 732 (23.60) | 460 (25.30) | 272 (21.10) | 0.006 |
| Hypertension, n (%) | 1391 (44.80) | 553 (30.50) | 838 (64.90) | <0.001 |
| Diabetes mellitus, n (%) | 464 (14.90) | 140 (7.70) | 324 (25.10) | <0.001 |

Notes: Data are presented as mean ± SD or median (IQR) for continuous variables and percentage for dichotomous variables. ^aMedian (interquartile range).

Abbreviations: MetS, metabolic syndrome; BMI, body mass index; eGFR, estimated glomerular filtration rate; SBPm, mean systolic blood pressure; DBPm, mean diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

adjustment for age, sex, and eGFR, with an odds ratio (OR) (95% confidence interval [CI]) of 1.69 (1.28, 2.23), and this relationship remained statistically significant after adjustment for other covariates, with an OR (95% CI) of 1.78 (1.34, 2.35). Of the individual components of the MetS, waist circumference, triglycerides, blood pressure, and fasting plasma glucose were all associated with the risk of rapid eGFR decline, with ORs (95% CI) of 1.38 (1.04, 1.83), 1.40 (1.05, 1.86), 2.05 (1.49, 2.82), 2.12 (1.57, 2.85), and 1.26 (0.94, 1.69), respectively, but HDL-C was not. Among these five components, high fasting plasma glucose and blood pressure carried the greatest risks of rapid eGFR decline.

The relationship between the number of MetS components present and rapid eGFR decline is presented in Table 3. The risk of rapid eGFR decline increased as the number of MetS components increased, with ORs (95% CIs) for one, two, three, four, and five components of 1.27 (0.68, 2.35), 1.94 (1.09, 3.47), 1.95 (1.07, 3.55), 3.47 (1.92, 6.29), and 3.19 (1.64, 6.22), respectively.

The results of subgroup analyses are displayed in Table 4. No significant heterogeneity was observed with regard to nearly all the parameters tested: sex, age (<65 or \geq 65 years), eGFR (<90 or \geq 90 mL/min/1.73 m²), current drinking (no or yes), or LDL-C (<3.4 or \geq 3.4 mmol/L). However, the OR for rapid eGFR decline was significantly higher in participants who were current smokers (*P*-interaction=0.030).

Discussion

The present study has shown that the presence of the MetS, individual components of the MetS, and the number of components present are independently associated with the risk of rapid eGFR decline in members of a Chinese community with eGFR $\geq 60 \text{ mL/min}/1.73 \text{ m}^2$. This finding is consistent with that of a previous prospective study performed in an Asian population.⁹

The MetS was found to be an important risk factor for deteriorating renal function. Recent studies have shown that the MetS plays an important role in the progression of CKD.11 Huh et al have reported that individuals with the MetS has a higher risk of CKD after adjustment for potential confounders (OR: 1.38, 95% CI: 1.16-1.64). They also found that the MetS is positively associated with the risk of a rapid decline in eGFR (OR: 1.20, 95% CI: 1.04-1.39).¹² In addition, the Jackson Heart study showed a positive relationship between the severity of the MetS and a rapid eGFR decline in African-American women.²⁶ Furthermore, a recent study derived from the Aichi Cohort Study of Prognosis in Patients Newly Initiated into Dialysis revealed that the rapidity of the decline in kidney function, which is similar to rapid eGFR decline, is positively correlated with all-cause mortality and CVD-related mortality.²⁷ However, Cheng et al have reported a negative association between rapid eGFR decline and the MetS, with an OR of 1.04 (95% CI: 0.80-

| Variables | Rapid eGFR Model I | | Model II | | Model III | | |
|--|-------------------------|------------------------|----------|------------------------|-----------|------------------------|---------|
| | Decline, n(%) | OR (95% CI) | P-value | OR (95% CI) | P-value | OR (95% CI) | P-value |
| MetS | | | | | | | |
| No | 104 (5.73) | 1 | | 1 | | | |
| Yes | 121 (9.37) | 1.69 (1.28, 2.23) | <0.001 | 1.78 (1.34, 2.35) | <0.001 | | |
| MetS components Waist circumference | | | | | | | |
| <90/80 cm (M/F) | 99 (6.24) | 1 | | 1 | | 1 | |
| ≥90/80 cm (M/F) | 126 (8.38) | 1.30 (0.98, 1.72) | 0.07 | 1.38 (1.04, 1.83) | 0.027 | 1.13 (0.84, 1.53) | 0.415 |
| Triglycerides | | | | | | | |
| <1.7 mmol/L | 133 (6.64) | 1 | | 1 | | 1 | |
| ≥I.7 mmol/L | 91 (8.40) | 1.31 (0.99, 1.73) | 0.057 | 1.40 (1.05, 1.86) | 0.022 | 1.18 (0.84, 1.66) | 0.328 |
| or on treatment | | | | | | | |
| HDL cholesterol ≥1.0/1.3 mmol/L(M/F) <1.0/1.3 mmol/L(M/F) or on treatment | 142 (6.55) 79 (8.66) | l 1.30 (0.97, 1.73) | 0.080 | l 1.26 (0.94, 1.69) | 0.117 | l 0.97 (0.68, 1.38) | 0.866 |
| Blood pressure <130/85 mm Hg ≥130/85 mm Hg or on medication | 60 (4.89) 163 (8.71) | .97 (.44, 2.7) | <0.001 | l 2.05 (1.49, 2.82) | <0.001 | l I.83 (I.32, 2.55) | <0.001 |
| Fasting plasma glucose <5.6 mmol/L ≥5.6 mmol/L or known diabetic | 76 (5.12) 148 (9.33) | l 2.06 (1.53, 2.76) | <0.001 | l 2.12 (1.57, 2.85) | <0.001 | l 1.82 (1.34, 2.47) | <0.001 |

| Table 2 The Relationships Of MetS And Its Components With Rapid eGFR Decline |
|---|
|---|

Notes: Model I: adjusted for age, sex, and eGFR. Model II: adjusted for age, sex, eGFR, smoking, drinking, and LDL-C. Model III: the five MetS components were included together, and adjusted for age, sex, eGFR, smoking, drinking, and LDL-C.

Abbreviations: OR, odds ratio; CI, confidence interval; MetS, metabolic syndrome; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

| Table 3 The Relationships Between The Number | Of MetS Components And Rapid eGFR Decline |
|--|---|
|--|---|

| Variables Rapid eGFR | | Crude Model | | Model I | | Model II | |
|----------------------|---------------|-------------------|---------|-------------------|---------|-------------------|---------|
| | Decline, n(%) | OR (95% CI) | P-value | OR (95% CI) | P-value | OR (95% CI) | P-value |
| MetS components | | | _ | | _ | | |
| 0 | 17 (4.49) | 1 | | 1 | | 1 | |
| I | 32 (4.83) | 1.08 (0.59, 1.98) | 0.798 | 1.14 (0.62, 2.09) | 0.671 | 1.27 (0.68, 2.35) | 0.455 |
| 2 | 55 (7.10) | 1.63 (0.93, 2.84) | 0.088 | 1.74 (0.99, 3.07) | 0.053 | 1.94 (1.09, 3.47) | 0.025 |
| 3 | 44 (6.93) | 1.59 (0.89, 2.82) | 0.116 | 1.68 (0.94, 3.00) | 0.081 | 1.95 (1.07, 3.55) | 0.029 |
| 4 | 52 (11.63) | 2.80 (1.59, 4.94) | 0.001 | 2.99 (1.68, 5.32) | <0.001 | 3.47 (1.92, 6.29) | <0.001 |
| 5 | 25 (11.90) | 2.88 (1.52, 5.46) | 0.001 | 2.94 (1.53, 5.66) | 0.001 | 3.19 (1.64, 6.22) | <0.001 |
| P for trend | | <0.001 | | <0.001 | | <0.001 | |

Notes: Model I: adjusted for age, sex, and eGFR. Model II: adjusted for age, sex, eGFR, smoking, drinking, and LDL-C. Abbreviations: OR, odds ratio; CI, confidence interval; MetS, metabolic syndrome.

1.36) after adjustment for covariates.²³ Therefore, therapy aimed at reducing the rate of renal deterioration may represent an alternative approach to reducing the risks of

all-cause and CVD-related mortality. Although the relationship between the MetS and CKD has been extensively studied, few prospective studies have been conducted in

| Characteristic | Rapid eGFR Decline, n(%) | OR (95% CI) | P-value | P-Interaction |
|--------------------------------------|--------------------------|-------------------|---------|---------------|
| Age (years) | | | | 0.432 |
| <65 | 185 (6.96) | 1.89 (1.39, 2.57) | <0.001 | |
| ≥65 | 40 (9.07) | 1.40 (0.70, 2.82) | 0.345 | |
| Sex | | | | 0.799 |
| Male | 61 (5.62) | 1.88 (1.11, 3.16) | 0.018 | |
| Female | 164 (8.14) | 1.70 (1.21, 2.39) | 0.002 | |
| eGFR, mL/min per 1.73 m ² | | | | 0.362 |
| ≥90 | 193 (7.06) | 1.92 (1.42, 2.61) | <0.001 | |
| <90 | 32 (8.77) | 1.00 (0.46, 2.15) | 0.999 | |
| Current smoking | | | | 0.030 |
| No | 195 (7.78) | 1.57 (1.16, 2.13) | 0.004 | |
| Yes | 30 (5.06) | 3.78 (1.68, 8.49) | 0.001 | |
| Current drinking | | | | 0.148 |
| No | 213 (8.99) | 1.94 (1.42, 2.65) | <0.001 | |
| Yes | 12 (1.65) | 1.11 (0.56, 2.18) | 0.764 | |
| LDL-C, mmol/L | | | | 0.932 |
| <3.4 | 141 (7.68) | 1.82 (1.28, 2.61) | 0.001 | |
| ≥3.4 | 82 (6.49) | 1.63 (1.02, 2.59) | 0.040 | |

 Table 4 Effect Of The Metabolic Syndrome On The Risk Of Rapid eGFR Decline By Subgroups

Notes: The model was adjusted for age, sex, eGFR, smoking, drinking, and LDL-C.

Abbreviations: OR, odds ratio; CI, confidence interval; HDL, high-density lipoprotein; LDL-C, low-density lipoprotein-cholesterol; BMI, body mass index.

patients from mainland China, and rapidity of the decline in kidney function has not typically been assessed. To our knowledge, this is the first community-based prospective study to determine the relationship between the MetS and a rapid decline in eGFR in China.

In the present study, nearly all the individual components of the MetS were found to be positively associated with the risk of rapid eGFR decline, with the exception of HDL-C. The results of previous similar studies conducted in different populations have been contradictory. For instance, the Arkhangelsk study showed that hypertension was a key contributory factor to cardiovascular disease in a Russian population.²⁸ In contrast, another recent study showed that only high fasting glucose (OR: 1.52, 95% CI: 1.12-2.05) was significantly associated with a reduction in renal function, after adjustment for age, sex, current smoking, current drinking, uric acid concentration, and all the other components of the MetS.9 Furthermore, Ding et al found that a high concentration of circulating triglyceride was strongly associated with CKD (hazard ratio: 1.14, 95% CI: 1.08-1.21).²⁹ Other studies have shown that a reduction in HDL-C is associated with a significantly higher risk of CKD.³³

High FBG and BP are shown to be the two components of the MetS with the largest ORs for a rapid decline in

eGFR: 2.12 (1.57, 2.85) and 2.05 (1.49, 2.82), respectively. These results indicate that high FBG and BP are more reliable predictors of rapid eGFR decline than the MetS itself. The possible explanation may be that our participants were part of a community-based population mainly accompanied with diabetes and/or hypertension, both of which are the main causes of kidney disease and may be associated with a higher risk of rapid eGFR decline. The Jackson Heart Study of 4933 African-Americans also showed that high BP, FBG, triglycerides, and abdominal obesity are significantly associated with the risk of CKD. However, the risks of CKD associated with high FBG and BP were higher than those associated with the other components of the MetS (OR [95% CI]: 4.41 [2.99–6.49] and 1.99 [1.60–2.47], respectively).³⁰

A graded relationship has previously been identified between the risk of CKD and the number of components of the MetS present. A cross-sectional study of older adult Japanese community-dwelling women showed that the number of MetS components is associated with the prevalence of CKD in non-obese subjects.³¹ Moreover, Okada et al found that both early- and late-stage kidney pathology increased with the number of MetS components present and that this association was statistically significant in both normal-weight and overweight individuals.³² Therefore, it seems that a combination of MetS components plays an active role in the deterioration of kidney function.

The present study has also revealed a positive relationship between the number of MetS components and rapid eGFR decline, consistent with the findings of previous studies.²⁰ Participants with five components of the MetS had an OR (95% CI) of 3.19 (1.64, 6.22) in the fully adjusted model, which represented a similar level of risk to that identified in another study.⁹ We can infer that a combination of MetS components, regardless of their identity, might increase the risk of kidney dysfunction. Thus, in clinical practice, the presence of any MetS component should provoke an appropriate intervention, even if the diagnostic criteria for the MetS are not met.

The subgroup analyses identified an interaction between the MetS and current smoking with regard to the risk of rapid eGFR decline because the OR for rapid eGFR decline associated with the MetS was significantly higher in participants who were current smokers (*P*-interaction=0.030). There could be two explanations for this finding. First, cell culture studies have repeatedly shown that nicotine-induced mesangial cell proliferation impairs their function, and kidney biopsies of active smokers demonstrate histopathologic changes,^{13,14} and second, smoking promotes local oxidative stress.^{15,16}

Several limitations of the present study should be noted. First, the participants were only followed for a median of 2.34 years, which may have limited the magnitude of the effect observed; therefore, a study containing a larger number of participants with this problem may be required to validate the identified relationship. Second, few covariates were adjusted for other than the components of the MetS; therefore, it was not possible to determine whether the presence of the MetS, independent of its single components, was associated with the risk of rapid eGFR decline. Finally, our study contained only Chinese participants, and therefore, the results may not be generalizable to other populations.

Conclusions

This study has shown that the MetS and its individual components are significantly associated with the risk of rapid eGFR decline in a population with normal renal function. In addition, we have shown that the risk of rapid eGFR decline increases with the number of MetS components present. High FBG and BP were the two most significant risk factors.

Abbreviations

MetS, metabolic syndrome; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; HDL-C, high-density lipoprotein-cholesterol; BP, blood pressure; BMI, body mass index; LDL-C, low-density lipoprotein-cholesterol.

Ethics Approval And Informed Consent

The participants gave their written informed consent. The study protocol was approved by the Ethics Committees of both Peking University and Peking University First Hospital (approval numbers: IRB00001052-11086; date: 2013-12-31) and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions

Conception and design: YZ, FF, JL, YH, JJ, YJ, DH, PS, and ZW. Acquisition of data: FF, JJ, YJ, DH, PS, and ZW. Analysis and interpretation of data: FF, JJ, PS, and ZW.

Drafting of the article: ZW. Revision of the article: YZ, FF, JL, YH, JJ, YJ, DH, PS, and ZW. The final manuscript has been reviewed and approved by all authors. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Disclosure

The authors report no conflicts of interest in this work.

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