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Original Article

Dose-Response Relationship of Serum Uric Acid and Incidence of Metabolic Syndrome and Components: A 4-Year Prospective Cohort Study

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SUMMARY

Background: The incidence of metabolic syndrome (MetS) dramatically increases among middle-aged and elderly populations in China, which increases the risk of cardiovascular disease events and mortality.
Methods: This survey was based on the China Health and Retirement Longitudinal Study baseline data in 2011 and follow-up data in 2015. 4,602 participants without MetS at baseline were included in the final analysis. The diagnosis of MetS was based on the Chinese guidelines. A multivariable logistic regression model was used to examine the association of serum uric acid quartiles, or continuous serum uric acid with the risk of incident MetS. Restricted cubic spline regression models were used to explore the dose–response relationship between serum uric acid levels and MetS incidence.
Results: Serum uric acid quartiles were associated with an increased risk of MetS incidence (p for trend = 0.03), and the adjusted RRs (95% CI) were 1.17 (0.77, 1.75), 1.51 (1.01, 2.24) and 1.54 (1.01, 2.33) in quartiles 2–4, respectively. In particular, the association was more evident among women. The multivariable-adjusted RR for 1 mg/dL in serum uric acid level was 1.17 (95% CI: 1.03, 1.34) for MetS incidence. In addition, the restricted cubic splines showed that higher serum uric acid levels were dose–response associated with increased MetS incidence risk (p for linear trend < 0.001).
Conclusions: Our results suggested that higher serum uric acid levels were independently associated with a dose-response increased risk of MetS incidence.

1. Introduction

Metabolic syndrome (MetS) is characterized by a clustering of cardiovascular disease (CVD) risk factors, stimulating early development of atherosclerosis and accelerating the frequency of CVD.[1] The prevalence of MetS dramatically increases worldwide[2,3] and has become a serious social health problem. The prevalence of MetS among participants aged 20 years and older was 31.1% based on the China Nutrition and Health Surveillance (2015– 2017) data by NCEP ATP III criteria.[4] Populations with MetS are at increased risk of CVD events,[5] especially elderly individuals. Overall, the age-standardized CVD prevalence rate significantly increased from 1990 to 2016 by 14.7% among Chinese residents based on the 2016 Global Burden of Disease Study data.[6] Exploring the risk factors for MetS may have important implications for preventing and controlling CVD in China, which has a large and aging population.

Uric acid is the final oxidation product of purine metabolism in the human body, and is used to define gout and assess renal function. Uric acid functions as a pro-oxidant within cells. Studies have demonstrated that increased serum uric acid levels stimulate oxidative stress, inflammation, and fat storage, suggesting a possible mechanism of metabolic homeostasis.[7,8] Several cross-sectional[9] and prospective[10] studies consistently demonstrated that elevated serum uric acid levels were related to an increased risk of MetS. Evidence also suggested the causal association between elevated serum uric acid and MetS and its components the Mendelian randomization method.[11]

CVD remains the leading cause of death in many developing countries, including China, with large aging populations. Hyperuricemia is common in the Chinese population, and the prevalence of hyperuricemia is higher in elderly populations.[12] Exploring the relationship between uric acid and MetS may have important implications for preventing and controlling MetS, which is a more important remediable risk factor for CVD. Therefore, in the present study, we tested the hypothesis that serum uric acid was dose–response associated with incident MetS among participants aged more than 45 years.

2. Materials and method

2.1. Study population

The China Health and Retirement Longitudinal Study (CHARLS) is a national population-based survey conducted by the National School of Development of Peking University and involved 17,708 participants aged 45 years and older. The participants were selected using a four-stage, stratified, cluster random sampling method from

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150 counties in 28 provinces. Detailed information on CHARLS was published previously.[13] In total, 14,255 individuals (80.5% of those at baseline) completed the follow-up in 2015. Participants with missing MetS data at the baseline survey (n = 4,456) were excluded. Among 6,994 participants without MetS at baseline and further excluding individuals with missing data on MetS (n = 2,392) at the follow-up investigation. A total of 4,602 participants aged 45 years and older were included in the final analysis (Figure 1). The CHARLS was approved by the Ethical Review Committee of Peking University. Informed consent was obtained from all individual participants included in the study.

2.2. Assessment of uric acid

Serum uric acid was determined at the Youanmen Center for Clinical Laboratory of Capital Medical University using the UA Plus method. Serum uric acid levels were categorized into four groups according to the quartiles of sex-specific distribution: < 3.96, 3.96–4.66, 4.66–5.50, and ≥ 5.50 mg/dL for men and 3.15, 3.15–3.70, 3.70–4.32, and ≥ 4.32 mg/dL for women.

2.3. Assessment of covariates

Trained interviewers used a semistructured questionnaire to collect data including demographic characteristics, lifestyle, and personal disease history during face-to-face interviews. Fasting blood glucose and lipids including total cholesterol (TC), and triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were measured by enzymatic colorimetric tests. Creatinine and C-reactive protein (CRP) were measured by the rate-blanked and compensated Jaffe creatinine method and immunoturbidimetric assay test, respectively. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) equations for the Chinese population with chronic kidney disease (CKD): eGFR = 186 × serum creatinine$^{-1.154}$ × Age$^{-0.203}$ × 0.742 (if female).[14]

2.4. Ascertainment of incident MetS

The diagnosis of MetS was based on the Chinese guidelines and included three or more of the following:[15] (1) abdominal obesity (defined according to guidelines for Chinese populations as a waist circumference ≥ 90 cm in men or ≥ 85 cm in women); (2) TG ≥ 150 mg/dL; (3) HDL-C cholesterol < 40 mg/dL; (4) systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or use of antihypertensive medications; and (5) fasting plasma glucose ≥ 110 mg/dL or use of antidiabetic medications.

2.5. Statistical analyses

Continuous variables with a normal distribution are presented as the means (SD) and were compared between groups using one-way ANOVA. Categorical variables are expressed as numbers (percentages) and were compared by the chi-square test. A multivariable logistic regression model was used to examine the association of serum uric acid quartiles with the risk of incident MetS. Additionally, the nonlinear relationship between serum uric acid levels and risk of incident MetS was evaluated by restricted cubic spline using 4 knots (5th, 35th, 65th, and 95th of the serum uric acid distribution) with 3 mg/dL (approximately the first quartile) as the reference. A 2-sided p value < 0.05 was used to determine statistical significance. Data cleaning and statistical analyses were performed using SAS version 9.2 (SAS Institute).

3. Results

3.1. Characteristics of study population

The general characteristics of the participants across sex-specific quartiles of serum uric acid levels are shown in Table 1. Compared with those in the first quartile, participants in the 2nd–4th quartiles were older and more likely to be current drinkers. High serum uric acid levels were associated with increased BMI, waist circumference, blood pressure, TC, TG, LDL-C, and creatinine, but with decreased eGFR. From serum uric acid level quartiles 1–4, MetS incidences were 10.10%, 10.92%, 13.57%, and 16.78% respectively.

3.2. Incidence of MetS and its components

The overall and sex-specific incident of MetS and its components at follow-up are shown in Figure 2. The difference between

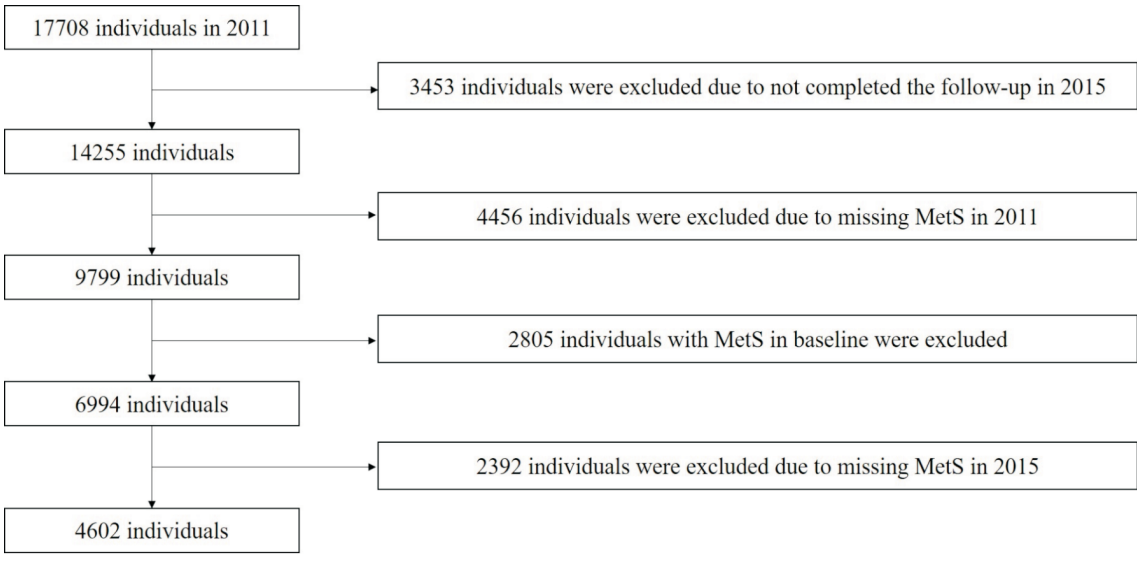

Figure 1. Flowchart of the study participant selection methods in each step.

Table 1
General characteristics of the subjects across quartiles of serum uric acid levels.

Variables	Quartiles of serum uric acid (mg/dL)				*p*-value
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
N	1148	1154	1150	1150	
Uric acid (mg/dL)					
Men	3.43 (0.43)	4.32 (0.20)	5.03 (0.24)	6.38 (0.89)	< 0.001
Women	2.71 (0.35)	3.43 (0.16)	3.99 (0.17)	5.09 (0.73)	< 0.001
Age (years)	57.69 (8.82)	58.12 (9.00)	58.56 (9.04)	59.93 (9.33)	< 0.001
Gender					0.95
Men	546 (47.56)	538 (46.62)	549 (47.74)	544 (47.30)	
Women	602 (52.44)	616 (53.38)	601 (52.26)	606 (52.70)	
Smoking, n (%)					0.55
Current	382 (33.33)	370 (32.17)	347 (30.33)	360 (31.47)	
Ever	78 (6.81)	85 (7.39)	97 (8.48)	97 (8.48)	
Never	686 (59.86)	695 (60.43)	700 (61.19)	687 (60.05)	
Drinking, n (%)					< 0.001
Current	263 (22.91)	287 (24.91)	319 (27.79)	340 (29.59)	
Ever	50 (4.36)	56 (4.86)	74 (6.45)	74 (6.44)	
Never	835 (72.74)	809 (70.23)	755 (65.77)	735 (63.97)	
BMI (kg/m^2)	22.29 (3.09)	22.32 (3.17)	22.68 (3.01)	22.98 (3.45)	< 0.001
Waist circumference (cm)	81.50 (8.24)	81.83 (8.65)	82.75 (8.64)	83.64 (9.54)	< 0.001
SBP (mmHg)	124.23 (21.34)	125.11 (22.06)	126.84 (22.87)	129.12 (22.51)	< 0.001
DBP (mmHg)	73.05 (11.15)	73.02 (11.67)	73.98 (12.12)	74.73 (11.65)	< 0.001
FPG (mmol/L)	104.01 (31.73)	102.00 (22.39)	101.97 (18.62)	102.51 (19.92)	0.13
HbAc1	5.17 (0.78)	5.15 (0.52)	5.13 (0.49)	5.14 (0.55)	0.34
TC (mg/dL)	183.58 (35.47)	189.42 (34.47)	191.81 (36.24)	196.96 (37.63)	< 0.001
TG (mg/dL)	95.11 (43.47)	95.89 (43.92)	102.57 (53.62)	109.76 (57.45)	< 0.001
LDL-C (mmol/L)	112.17 (30.90)	116.07 (30.32)	117.39 (33.06)	121.22 (35.15)	< 0.001
HDL-C (mmol/L)	54.64 (13.74)	56.11 (14.62)	55.78 (14.40)	55.02 (14.39)	0.05
Creatinine (mg/dL)	0.69 (0.15)	0.74 (0.15)	0.77 (0.16)	0.85 (0.21)	< 0.001
CRP (mg/L)	2.11 (6.22)	2.25 (7.27)	2.12 (6.92)	2.66 (6.26)	0.16
eGFR	112.97 (24.25)	102.53 (22.00)	97.99 (19.00)	88.75 (20.81)	< 0.001
MetS, n (%)	116 (10.10)	126 (10.92)	156 (13.57)	193 (16.78)	< 0.001

Abbreviation: BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.

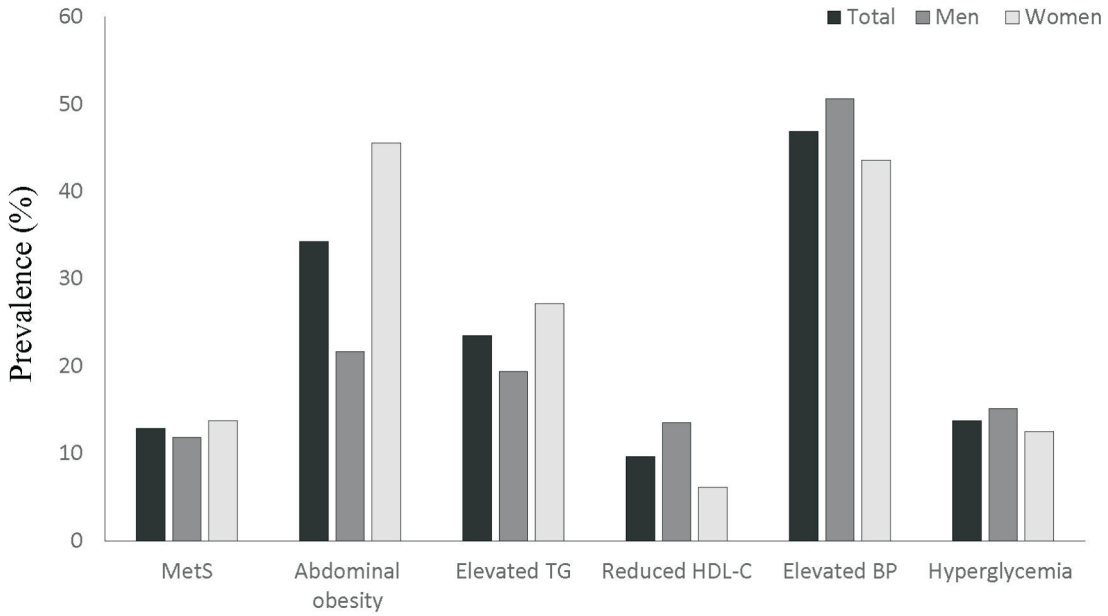

Figure 2. The overall and sex-specific incidence of MetS and its components at follow-up. MetS, metabolic syndrome; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; BP, blood pressure.

men and women is expressed as the *p*-value calculated by chi-square test. The 4-year follow-up MetS incidence was 12.84% in all participants. The MetS incidence was significantly higher in women (13.77%) than in men (11.81%) ($p = 0.04$). MetS components, such as abdominal obesity and elevated TGs were significantly higher in women than in men ($p < 0.001$ for all cases). In contrast, the incidence of reduced HDL-C, elevated BP, and hyperglycemia was significantly lower in women than in men ($p < 0.01$ for all cases).

3.3. Relationship between serum uric acid and MetS incidence

Table 2 shows the risk ratios (95% CIs) for the incidence of MetS and its components according to quartiles of serum uric acid. We found that higher serum uric acid quartiles were independently associated with increased MetS incident risk after adjustment for confounding factors. Compared with the first quartile of serum uric acid levels, the adjusted RRs (95% CIs) of MetS incidence were 1.17 (95% CI: 0.77, 1.75), 1.51 (95% CI: 1.01, 2.24) and 1.54 (95% CI: (1.01, 2.33); p for trend = 0.03) respectively in 2–4 quartiles. The multivariable-adjusted RR for 1 mg/dL in serum uric acid levels was 1.17 (95% CI: 1.03, 1.34) for MetS incidence.

The restricted cubic splines showed that the risk of MetS incidence increased with continuous serum uric acid levels (p for linear trend < 0.001, Figure 3a). The significant linear trend test illustrated dose–response effects and no obvious evidence of a threshold effect on the risk of MetS incidence. In contrast, a significant nonlinear relationship existed between serum uric acid levels and the risk of abdominal obesity and elevated TG incidence based on restricted cubic spline regression models (p for nonlinear trend < 0.05 for both; Figure 3b and 3c).

4. Discussion

In this population-based prospective study, our findings demonstrated that dose–response positive association between serum uric acid and MetS incidence risk among middle-aged and elderly Chinese adults after adjustment for a variety of confounding factors.

Our findings showed that participants in the highest quartile had a 1.54-fold risk of MetS incidence compared with those in the first quartile. Higher serum uric acid levels dose–response associated with increased risk of MetS incidence. The potential mechanisms for the hyperuricemia-MetS association are that serum uric acid in adipocytes leads to inflammation and oxidative stress, which cause insulin resistance and the development of metabolic diseases.[16] Consistently, several prospective studies conducted among Chinese populations suggested positive associations between serum uric acid levels and MetS incident risk.[17,18] In addition, previous studies demonstrated that hyperuricemia is independently associated with CVDs, hypertension, obesity, type 2 diabetes mellitus, and stroke.[19–22] A nationally representative study – the China Nutrition and Health Surveillance (CNHS) showed that the uric acid level in Chinese adults is relatively high.[23] Early intervention and control of hyperuricemia may have important implications for preventing and controlling chronic diseases.

In the present study, we also found that higher serum uric acid levels are associated with an increased risk of abdominal obesity and dyslipidemia but not hypertension and hyperglycemia, which is in accordance with the results of other studies.[24,25] A possible explanation for the association between uric acid and obesity may be that uric acid levels are associated with risk factors for obesity, such as insulin resistance and dyslipidemia. Obesity is related to oxidative stress, and uric acid helps the clearance of free radicals in the obese body. On the other hand, the increase in uric acid cannot be completely removed, leading to hyperuricemia.[26] This suggested that the association between obesity and hyperuricemia may be bidirectional. To date, the mechanisms underlying the association between uric acid and hypertriglyceridemia have not been fully elucidated. A study suggested that increased serum uric acid levels may inhibit the decomposition of serum TG by reducing the activity of enzymes as-

Table 2
Risk ratios (95% CIs) for MetS incidence according to continuous or quartiles of serum uric acid.

	Quartiles of serum uric acid (mg/dL)				p-trend*	Per 1 mg/dL increase	p-value
	Quartile 1	Quartile 2	Quartile 3	Quartile 4			
MetS							
Model 1	reference	1.09 (0.84,1.42)	1.40 (1.08,1.80)	1.79 (1.40,2.30)	< 0.001	1.17 (1.09,1.25)	< 0.001
Model 2	reference	1.16 (0.77,1.73)	1.49 (1.01,2.19)	1.51 (1.03,2.23)	0.02	1.16 (1.03,1.31)	0.01
Model 3	reference	1.17 (0.77,1.75)	1.51 (1.01,2.24)	1.54 (1.01,2.33)	0.03	1.17 (1.03,1.34)	0.02
Abdominal obesity							
Model 1	reference	1.08 (0.90,1.29)	1.37 (1.15,1.63)	1.50 (1.26,1.78)	< 0.001	1.20 (1.13,1.27)	< 0.001
Model 2	reference	1.07 (0.81,1.41)	1.55 (1.18,2.04)	1.47 (1.12,1.94)	0.002	1.16 (1.06,1.27)	0.002
Model 3	reference	1.05 (0.79,1.39)	1.51 (1.14,1.99)	1.47 (1.09,1.97)	0.003	1.17 (1.06,1.29)	0.002
Elevated BP							
Model 1	reference	1.11 (0.94,1.30)	1.37 (1.16,1.61)	1.46 (1.24,1.72)	< 0.001	1.19 (1.13,1.25)	< 0.001
Model 2	reference	1.10 (0.85,1.44)	1.27 (0.98,1.66)	1.17 (0.90,1.53)	0.23	1.06 (0.97,1.16)	0.19
Model 3	reference	1.12 (0.85,1.46)	1.30 (0.99,1.71)	1.22 (0.92,1.62)	0.18	1.08 (0.98,1.18)	0.14
Elevated TG							
Model 1	reference	1.22 (1.00,1.50)	1.46 (1.20,1.78)	1.77 (1.45,2.15)	< 0.001	1.08 (1.02,1.14)	0.006
Model 2	reference	1.18 (0.86,1.62)	1.50 (1.10,2.04)	1.67 (1.23,2.27)	< 0.001	1.17 (1.06,1.30)	0.002
Model 3	reference	1.13 (0.82,1.56)	1.42 (1.03,1.94)	1.49 (1.07,2.07)	0.01	1.12 (1.01,1.25)	0.03
Reduced HDL-C							
Model 1	reference	0.84 (0.63,1.12)	0.97 (0.74,1.28)	1.06 (0.81,1.39)	0.39	1.17 (1.09,1.27)	< 0.001
Model 2	reference	1.11 (0.71,1.74)	1.41 (0.91,2.17)	1.40 (0.90,2.17)	0.11	1.06 (0.93,1.22)	0.37
Model 3	reference	1.15 (0.73,1.82)	1.48 (0.94,2.31)	1.48 (0.92,2.37)	0.08	1.07 (0.93,1.24)	0.39
Hyperglycemia							
Model 1	reference	0.99 (0.78,1.25)	0.79 (0.62,1.02)	1.17 (0.93,1.47)	0.17	1.07 (1.00,1.15)	0.05
Model 2	reference	0.86 (0.59,1.25)	0.69 (0.46,1.02)	1.15 (0.80,1.65)	0.33	1.08 (0.96,1.23)	0.20
Model 3	reference	0.89 (0.61,1.31)	0.72 (0.48,1.09)	1.22 (0.82,1.81)	0.23	1.11 (0.97,1.27)	0.13

Abbreviation: BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; TG, triglycerides.
* p values for trend were estimated by modelling the serum uric acid using the median for each quartile.
Model 1 adjusted for age and gender.
Model 2 further adjusted for drinking status (never, ever, or current), smoking status (never, ever, or current), and exercise (yes or no).
Model 3 further adjusted for BMI, eGFR, and CRP (all as continuous variables).

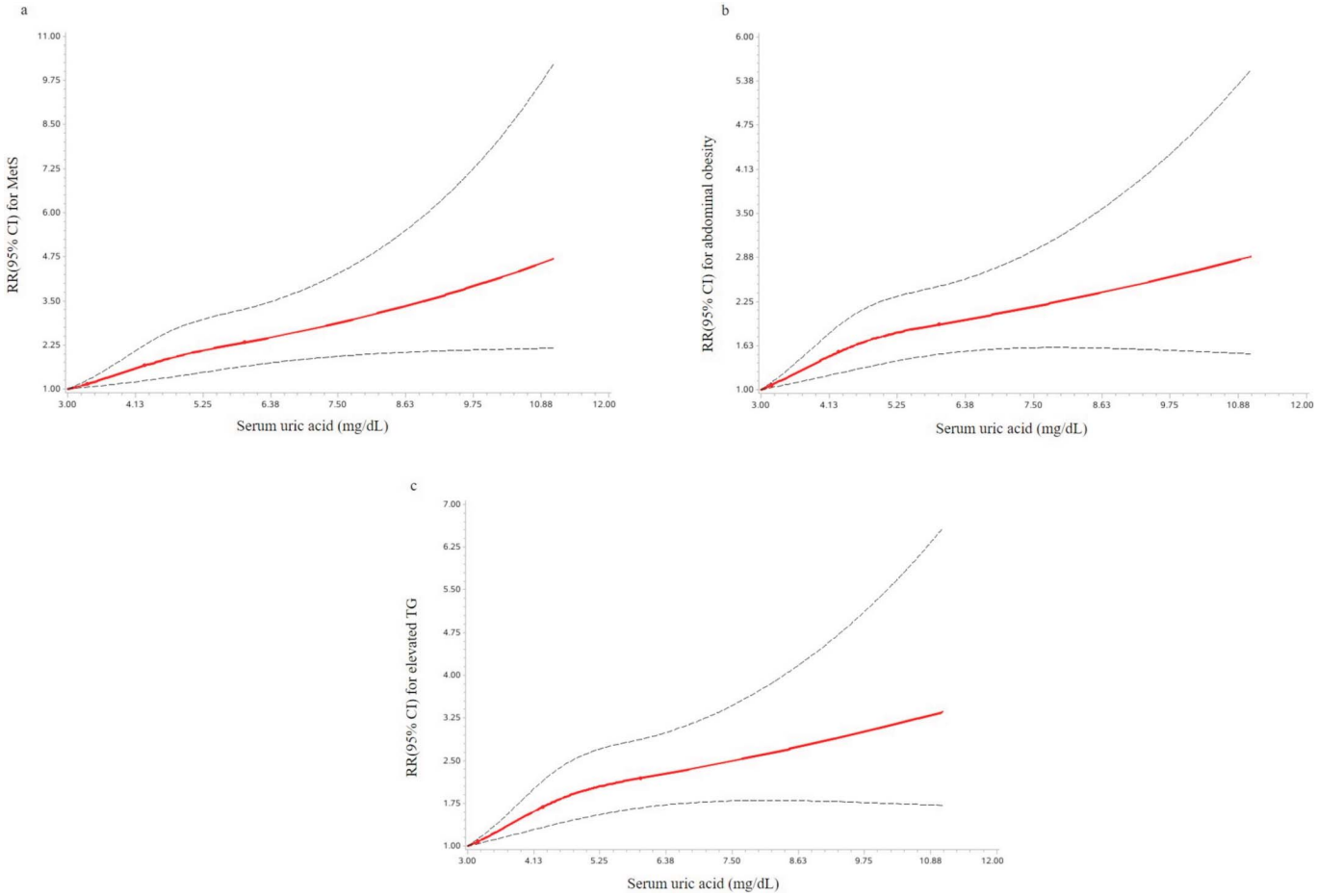

Figure 3. Adjusted RRs and 95% CIs for MetS, abdominal obesity and elevated TG incidence from restricted cubic splines. The solid line represents the fitted risk ratio curve compared to the subgroup with the lowest mean dose of uric acid, and the flanked dotted line is the 95% CI of this risk by the restricted cubic spline model. The model was adjusted for age, sex, alcohol consumption status, smoking status, exercise, BMI, eGFR, and CRP.

sociated with catalyzing TG decomposition, which leads to participants with higher serum uric acid levels with an increased incidence of hypertriglyceridemia.[27]

Our findings showed that the 4-year incidence of MetS, abdominal obesity, and hypertriglyceridemia was higher among women. Increased waist circumference and visceral adipose tissue further induce inflammation and oxidative stress, which cause an increased risk of MetS incidence in women. Sex differences in steroid hormones may influence the difference in abdominal accumulation among men and women. Women had a higher prevalence of abdominal obesity because pregnancy in the early period and the postmenopausal period may increase the amount and distribution of abdominal fat.[28] Our stratified analyses further showed that serum uric acid was associated with a greater RR value of MetS among women than men, but without a significant sex interaction, which is in accordance with another study conducted among individuals.[29]

This study has several strengths. First, our results are based on a population-based design, large sample size, prospective design, and structured questionnaire survey, which guarantees high statistical power to provide a more convincing result. Second, restricted cubic spline regression models further explored the dose–response association between serum uric acid and MetS incident risk. Nevertheless, potential limitations should be considered. First, participants included in the present study were middle-aged and elderly populations. The findings might not be generalizable to those younger than 45 years. Second, although the regression models were adjusted for a range of potential confounders, other unmeasured confounders such as diet, drugs, and genetics might modify the association between serum uric acid and MetS. Third, we only used the baseline serum uric acid levels, so we were unable to account for within-individual variability in this study. Finally, the 4-year follow-up period of this prospective cohort study is comparatively shorter than that of other prospective cohort studies.

In summary, our findings confirm hyperuricemia as an independent risk factor and show a positive dose–response relationship between serum uric acid levels and MetS incidence in middle-aged and older Chinese populations. Furthermore, our findings suggest that more efficient prevention strategies for hyperuricemia, which is a risk factor for cardiovascular and metabolic disease.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of

the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation.* 2005;112: 2735–2752. doi:10.1161/CIRCULATIONAHA.105.169404
2. Aguilar M, Bhuket T, Torres S, Liu B, Wong RJ. Prevalence of the metabolic syndrome in the United States, 2003-2012. *JAMA.* 2015;313:1973–1974. doi:10.1001/jama.2015.4260
3. Kim HJ, Kim Y, Cho Y, Jun B, Oh KW. Trends in the prevalence of major cardiovascular disease risk factors among Korean adults: results from the Korea National Health and Nutrition Examination Survey, 1998-2012. *Int J Cardiol.* 2014;174:64–72. doi:10.1016/j.ijcard.2014.03.163
4. Yao F, Bo Y, Zhao L, et al. Prevalence and influencing factors of metabolic syndrome among adults in China from 2015 to 2017. *Nutrients.* 2021;13: 4475. doi:10.3390/nu13124475
5. Gustavo de Sousa Barbalho Y, Morato Stival M, Ramos de Lima L, et al. Impact of metabolic syndrome components in high-risk cardiovascular disease development in older adults. *Clin Interv Aging.* 2020;15:1691–1700. doi:10.2147/CIA.S252589
6. Liu S, Li Y, Zeng X, et al. Burden of cardiovascular diseases in China, 1990-2016: Findings from the 2016 Global Burden of Disease Study. *JAMA Cardiol.* 2019;4:342–352. doi:10.1001/jamacardio.2019.0295
7. Lima WG, Martins-Santos ME, Chaves VE. Uric acid as a modulator of glucose and lipid metabolism. *Biochimie.* 2015;116:17–23. doi:10.1016/j.biochi.2015.06.025
8. Choi Y, Shin H, Choi H, et al. Uric acid induces fat accumulation via generation of endoplasmic reticulum stress and SREBP-1c activation in hepatocytes. *Lab Invest.* 2014;94:1114–1125. doi:10.1038/labinvest.2014.98
9. de Magalhães ELG, Juvanhol LL, da Silva DCG, et al. Uric acid: A new marker for metabolic syndrome? Results of a population-based study with adults. *Nutr Metab Cardiovasc Dis.* 2021;31:2077–2080. doi:10.1016/j.numecd.2021.03.012
10. Zhang S, Ma Z, Li Q, et al. Dose-response relationship between distinct serum uric acid trajectories and metabolic syndrome risk: A 5-year prospective cohort study. *Nutr Metab Cardiovasc Dis.* 2021;31:1189–1199. doi:10.1016/j.numecd.2020.12.007
11. Biradar MI, Chiang KM, Yang HC, Huang YY, Pan WH. The causal role of elevated uric acid and waist circumference on the risk of metabolic syndrome components. *Int J Obes (Lond)*. 2020;44:865–874. doi:10.1038/s41366-019-0487-9
12. Li Y, Shen Z, Zhu B, Zhang H, Zhang X, Ding X. Demographic, regional and temporal trends of hyperuricemia epidemics in mainland China from 2000 to 2019: a systematic review and meta-analysis. *Glob Health Action.* 2021;14:1874652. doi:10.1080/16549716.2021.1874652
13. Zhao Y, Hu Y, Smith JP, Strauss J, Yang G. Cohort profile: the China Health and Retirement Longitudinal Study (CHARLS). *Int J Epidemiol.* 2014;43: 61–68. doi:10.1093/ije/dys203
14. Ma YC, Zuo L, Chen JH, et al. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol.* 2006;17:2937–2944. doi:10.1681/ASN.2006040368
15. Joint committee for guideline revision. 2016 Chinese guidelines for the management of dyslipidemia in adults. *J Geriatr Cardiol*. 2018;15:1–29. doi:10.11909/j.issn.1671-5411.2018.01.011
16. Furukawa S, Fujita T, Shimabukuro M, et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest.* 2004;114: 1752–1761. doi:10.1172/JCI21625
17. Chen S, Wu N, Yu C, et al. Association between baseline and changes in serum uric acid and incident metabolic syndrome: a nation-wide cohort study and updated meta-analysis. *Nutr Metab (Lond).* 2021;18:59. doi: 10.1186/s12986-021-00584-x
18. Liu Y, Fan Y, Liu Q, et al. Sex-specific association of serum uric acid dynamics with the incidence of metabolic syndrome in a health check-up Chinese population: a prospective cohort study. *BMJ Open.* 2020;10: e035289. doi:10.1136/bmjopen-2019-035289
19. Saito Y, Tanaka A, Node K, Kobayashi Y. Uric acid and cardiovascular disease: A clinical review. *J Cardiol.* 2021;78:51–57. doi:10.1016/j.jjcc.2020.12.013
20. Sun P, Chen M, Guo X, et al. Combined effect of hypertension and hyperuricemia on ischemic stroke in a rural Chinese population. *BMC Public Health.* 2021;21:776. doi:10.1186/s12889-021-10858-x
21. Shirasawa T, Ochiai H, Yoshimoto T, et al. Correction to: Cross-sectional study of associations between normal body weight with central obesity and hyperuricemia in Japan. *BMC Endocr Disord.* 2020;20:26. doi:10.1186/s12902-020-0494-9
22. Ae R, Kanbay M, Kuwabara M. The causality between the serum uric acid level and stroke. *Hypertens Res.* 2020;43:354–356. doi:10.1038/s41440-019-0346-z
23. Piao W, Bo YC, Zhao LY, Yu DM. Status of serum uric acid and hyperuricemia among adults in China: China Nutrition and Health Surveillance (2015). *Biomed Environ Sci.* 2022;35:911–920. doi:10.3967/bes2022.118
24. Huang G, Xu J, Zhang T, et al. Hyperuricemia is associated with metabolic syndrome in the community very elderly in Chengdu. *Sci Rep.* 2020;10: 8678. doi:10.1038/s41598-020-65605-w
25. Liu M, He Y, Jiang B, et al. Association between serum uric acid level and metabolic syndrome and its sex difference in a Chinese community elderly population. *Int J Endocrinol.* 2014;2014:754678. doi:10.1155/2014/754678
26. Liu F, Chen S, Zhao W, et al. Urine uric acid excretion levels are positively associated with obesity and abdominal obesity in type 2 diabetes patients without chronic kidney disease. *Diabetes Metab Syndr Obes.* 2021; 14:4691–4703. doi:10.2147/DMSO.S335558
27. Zheng R, Ren P, Chen Q, Yang T, Chen C, Mao Y. Serum uric acid levels and risk of incident hypertriglyceridemia: A Longitudinal Population-based Epidemiological Study. *Ann Clin Lab Sci.* 2017;47:586–591.
28. Cisse K, Samadoulougou S, Ouedraogo M, Kouanda S, Kirakoya-Samadoulougou F. Prevalence of abdominal obesity and its association with cardiovascular risk among the adult population in Burkina Faso: findings from a nationwide cross-sectional study. *BMJ Open.* 2021;11: e049496. doi:10.1136/bmjopen-2021-049496
29. Huang G, Xu JB, Zhang TJ, et al. Hyperuricemia is associated with cardiovascular diseases clustering among very elderly women - a community based study in Chengdu, China. *Sci Rep.* 2017;7:996. doi:10.1038/s41598-017-01042-6