Original Article

Positive association between metabolic syndrome and serum uric acid in Wuhan

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Background and Objectives: The objective was to determine whether serum uric acid concentrations were associated with metabolic syndrome in a population from Wuhan. **Methods and Study Design:** 5,628 subjects (2,838 men, 2,790 women) aged 18-80 years were recruited in Wuhan, China. Biochemical parameters of venous blood were measured by standard methods and metabolic syndrome was defined by Chinese Diabetes Society criteria. Association analysis was performed by logistic regression. **Results:** 8.2% of the included subjects were confirmed as having metabolic syndrome and 14.4% were confirmed as having hyperuricemia. After multivariable adjustment, logistic regression showed the odds ratios of metabolic syndrome for subjects in the highest quartile of serum uric acid concentration was 2.84 (95% CI: 2.09-3.86) compared with those in the lowest quartile and no gender difference was found. For each component of metabolic syndrome, subjects in the highest quartile of serum uric acid concentrations had increased multivariable odds ratios for high BMI (OR: 3.29, 95% CI: 2.71-3.98), for hypertension (OR: 3.54, 95% CI: 2.93-3.86), for dyslipidemia (OR: 2.49, 95% CI: 1.98-3.14), but not for hyperglycemia (OR: 1.21, 95% CI: 0.87-1.67). **Conclusions:** Odd ratio of metabolic syndrome was significantly positively associated with serum uric acid concentration among the present sample of 5,628 subjects in Wuhan.

Key Words: metabolic syndrome, uric acid, cardiovascular risk, Wuhan population

INTRODUCTION

The characteristics of metabolic syndrome (MS) include obesity, hypertension, hyperglycemia and dyslipidemia, which are cardiovascular risk factors.[1] The prevalence of MS in China has been reported to be 9.8% for men and 17.8% for women based on a survey conducted in 2000-2001.[2] The prevalence of MS in United States is much higher (25.2% in men and 29% in women).[3] With more and more epidemiological evidence and systematic reviews suggesting that MS is associated with increased risk of cardiovascular diseases,[4,5] diabetes,[6] cancers,[7] and even osteoporosis,[8] MS has become a large public health issue worldwide as a result. On the other hand, serum uric acid (UA) is also drawing increased attention as a marker of inflammation. Many studies reported higher serum UA concentration as an important marker predicting the risk of developing CVD,[9,10] stroke,[11,12] cancer,[13] and acute coronary syndromes.[14] Moreover, increased serum UA level has also been reported to be associated with MS and its components such as hypertension, diabetes, obesity, and dyslipidemia.[15-19] Even though previous studies have examined the putative association between serum UA levels and the MS, one of the latest studies conducted in China was limited to subjects among retired employees (age older than 50 years) of a Motor Corporation.[19] Additionally, no study on this topic has been conducted in central China population. The present study with a representative sample of Wuhan adults examined the association between serum UA levels and MS and its components.

MATERIALS AND METHODS
Design and study population
A cross-sectional study was conducted among 5,628 subjects (2,838 men, 2,790 women) aged 18-80 years. The cases of MS and hyperuricemia were calculated and the association between serum UA level and the MS and its several components were examined.

Subjects were recruited through a general health screening program between September 2011 and February 2014 in Wuhan, China. The procedures of the health screening have been reported elsewhere. Briefly, they visited the Health Examination Centre, Wuhan Puai Hos-

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pital in the morning following an overnight fast. For each individual, after standard anthropometric examination, ten milliliters of fasting blood were drawn, from which serum UA and other parameters of biochemistry necessary to assess the presence or absence of MS were measured. Indexes deviating from normal reference ranges were considered as abnormal.

None of the included participants had thyroid, renal, hepatic, gastrointestinal, or oncology disease or were receiving drugs for hypoglycemia, antioxidant vitamin supplementation, or drugs known to affect lipoprotein metabolism or UA metabolism. As the mean UA level was found to be significantly lower in women compared with that in men, gender-specific quartiles of serum UA were used. The study was approved by the Research Ethical Committee, School of Biosystems Engineering and Food Science, Zhejiang University (ZJU-BEFS-2014008A). All subjects gave written informed consent.

Criteria for metabolic syndrome and hyperuricemia

Diagnosis of MS was made according to the criteria of Chinese Diabetes Society (CDS)[20] for Chinese when three or four of the following criteria are met: 1) high BMI, as body mass index (BMI) ≥25; 2) high blood pressure, as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg; or known treatment for hypertension; 3) dyslipidemia, as fasting triacyglycerol ≥1.7 mmol/L (150mg/dL), or high density lipoprotein cholesterol (HDL-C) <0.9 mmol/L (35 mg/dL) in men and <1.0 mmol/L (39 mg/dL) in women; 4) impaired insulin tolerance, as fasting glucose ≥6.1 mmol/L (109 mg/dL); or known treatment for diabetes. Hyperuricemia is defined by cut-off value of >420 μmol/L for men and >360 μmol/L for women.

Parameters measurement

The measurement methods have been reported previously. Briefly, Weight and height were measured on an auto-anthropometer (super-view, HW-666) and body mass index (BMI) was calculated by the formula of weight $(kg)/(height)^2(m^2)$. Blood pressure was measured by an electronic device (COLIN, VP-100, Japan) after the subjects sat relaxed for 10 min. Ten milliliters of fasting blood were drawn in the morning after at least a 10-hour overnight fasting and was sent for analysis within four hours of blood collection. Biochemical markers such as serum UA, triacylglycerol (TG) and total cholesterol (TC) concentrations were determined by standard enzymatic dipyridamole methods. High density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) were measured by differential antibody methods, and blood glucose was measured by hexokinase methods on an auto-biochemical analyzer (Olympus AV400, Japan). Lipoprotein, triacylglycerol, total cholesterol, blood glucose and urea nitrogen concentrations were reported as mmol/L, while UA and creatinine concentrations as μmol/L.

Statistical analyses

All continuous variables were examined for normal distribution and reported as mean±SD and categorical variables were expressed in percentages. Values with skewed
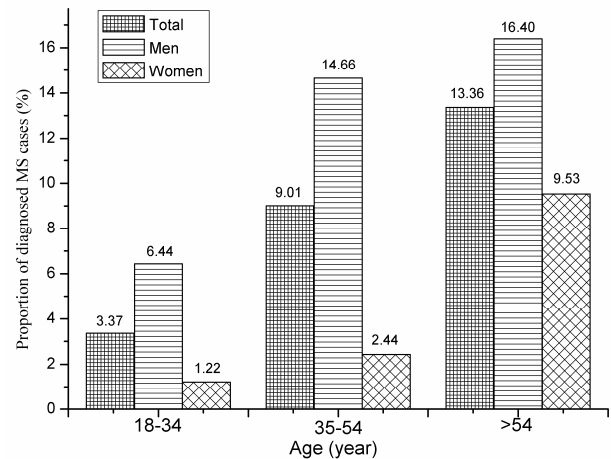

Figure 1. Proportion of diagnosed MS cases among 5628 subjects according to age distribution.

distribution (glucose and triacylglycerol) were transformed to their Ln forms for analyses. One-way Analysis of Variance (ANOVA) was used to assess the difference between subgroups. The chi-square test was used for categorical variables. Simple and multivariable adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the MS and its components were computed using the logistic regression and age (continuous), gender (men/women), concentration of hemoglobin (continuous), creatinine (continuous), red blood cell count (continuous) and white blood cell count (continuous) were adjusted in the multivariable model. All analyses were performed using the SPSS software package version 16.0 for windows (SPSS Inc., Chicago, IL, USA). Two-tailed p value <0.05 was considered significant.

RESULTS

Characteristics of the study subjects

A total of 5,628 individuals (2,838 men, 2,790 women) providing sufficient health examination data were included in this study and the characteristics of all subjects according to quartiles of UA concentration are summarized in Table 1. Subjects allocated in the highest quartile of UA concentration tended to be older and had higher blood pressure and BMI, and higher LDL-C, creatinine, urea nitrogen, hemoglobin, platelet count, red blood cell (RBC) and white blood cell (WBC) count (p<0.01 for all), but lower levels of HDL-C (p<0.01). Overall, 8.2% of the included subjects were confirmed as having metabolic syndrome and 14.4% were confirmed as having hyperuricemia, and both MS and hyperuricemia cases were much more likely observed among men than women (p<0.01) (Table 2). Figure 1 shows the proportion of MS cases among subjects with different age, which indicates that MS cases account for a larger proportion among subjects with older age than their counterparts (p<0.01). The distributions of serum UA concentration for all subjects is shown in Figure 2, in which 650 men and 159 women were confirmed as having hyperuricemia and these cases contributed to 22.9% and 5.7% of hyperuricemia for men and women, respectively. As significant differences of the serum UA concentration were found between the two gender subgroups (Table 2), gender-specific quartiles of

Table 1. Characteristics of included subjects according to quartiles of serum uric acid concentrations

Characteristics	Quartiles of serum uric acid (μmol /L)				p value
	Q_1	Q_2	Q_3	Q_4	
Sample size	1408	1407	1406	1407	-
Gender (men/women)	710/698	710/697	708/698	710/697	0.99
Age	43.4 (12.4)	41.8 (12.3)	42.6 (12.8)	44.0 (14.1)	<0.01
Blood pressure (mm Hg)					
Systolic	117 (17.4)	118 (17.4)	122 (18.7)	126 (20.3)	<0.01
Diastolic	71.7 (10.7)	72.6 (10.9)	74.0 (11.3)	76.5 (12.2)	<0.01
Body mass index (kg/m^2)	22.4 (3.1)	23.0 (3.3)	23.6 (3.3)	24.7 (3.3)	<0.01
Ln fasting blood glucose	1.60 (0.18)	1.60 (0.15)	1.60 (0.13)	1.61 (0.16)	<0.05
Ln triglyceride	0.05 (0.52)	0.15 (0.57)	0.25 (0.57)	0.44 (0.59)	<0.01
Total cholesterol (mmol/L)	4.51 (0.83)	4.61 (0.86)	4.70 (0.87)	4.88 (0.98)	<0.01
HDL-C (mmol/L)	1.22 (0.26)	1.20 (0.28)	1.19 (0.28)	1.14 (0.26)	<0.01
LDL-C (mmol/L)	2.75 (0.75)	2.81 (0.80)	2.85 (0.81)	2.96 (0.84)	<0.01
Creatinine (μmol /L)	69.1 (15.6)	73.5 (18.8)	75.7 (16.2)	79.8 (18.3)	<0.01
Urea nitrogen (mmol/L)	4.75 (1.27)	4.84 (1.28)	4.96 (1.21)	5.10 (1.24)	<0.01
Hemoglobin (g/L)	138 (15.5)	140 (15.9)	140 (15.0)	142 (15.4)	<0.01
Platelet count (10^9/L)	214 (51.2)	220 (55.5)	226 (52.6)	225 (57.1)	<0.01
Red blood cell count (10^{12}/L)	4.60 (0.45)	4.64 (0.48)	4.68 (0.48)	4.72 (0.48)	<0.01
White blood cell count (10^9/L)	5.80 (1.47)	5.97 (1.50)	6.08 (1.44)	6.36 (1.53)	<0.01
Uric acid (μmol/L)	239 (50.0)	292 (52.2)	331 (58.5)	407 (82.7)	<0.01

The quartiles of serum uric acid concentration were calculated sex-specifically. In men, the cutoff values of serum uric acid concentration are <320, 320-363, 364-413, and >413 μmol/L respectively; in women, the cutoff values are <224, 224.2-255, 226-294, and >294 μmol/L respectively. All continuous variables were reported as mean (SD, standard deviation).

Table 2. Gender-specific proportion of metabolic syndrome[†] cases (%) and serum uric acid concentration (μmol /L)

	High BMI	Hypertension	Hyperglycemia	Dyslipidemia	Metabolic syndrome	Uric acid
All subjects	1715 (30.5)	993 (17.6)	342 (6.1)	1842 (32.7)	461 (8.2)	317
Men	1232 (43.4)	681 (24.0)	238 (8.4)	1316 (46.4)	370 (13.0)	370
Women	483 (17.3)	312 (11.2)	104 (3.7)	526 (18.9)	91 (3.3)	263
p value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

[†]Metabolic syndrome and its components were diagnosed according to Chinese Diabetes Society (CDS) criteria for Chinese people.[20]

serum UA were used in the present study. As shown in Figure 3, there was a sharp increase in the proportion of MS cases from quartile 2 to quartile 4 for both men (from 13.1% to 20.0%) and women (from 3.4% to 7.7%).

Association between potential confounding factors of UA and metabolic syndrome

Individuals with older age (≥50 years) or abnormal blood hemoglobin and creatinine concentration, abnormal WBC and RBC count were more likely to suffer MS. The logistic regression analysis showed crude odds ratio (OR) of MS for subjects older than 50 was 2.41 (95% CI: 1.99, 2.92) compared with those younger than 50 years, for subjects with abnormal blood hemoglobin concentration the OR was 2.66 (95% CI: 1.53, 4.62), for subjects with abnormal creatinine concentration the OR was 4.53 (95% CI: 1.75, 11.73), for subjects with abnormal WBC count the OR was 2.82 (95% CI: 1.62, 4.92), and for subjects with abnormal RBC count it was 2.02 (95% CI: 1.37, 2.98). While for subjects with abnormal levels of BUN or platelet count, no significant higher odds ratios of MS were found. Therefore, age, gender, blood level of hemoglobin, creatinine, RBC count and WBC count were included in the multivariable model in the following analysis. For each component of MS, the evaluations of confounding factors are listed in Table 3.

Association between serum UA levels and metabolic syndrome

Logistic regression for the association between MS (or its components) and serum UA concentration by quartiles of UA distribution are shown in Table 4. The odds ratio of MS for subjects allocated in the highest quartile of UA concentration was 2.84 (95% CI: 2.09, 3.86) compared with those in the lowest quartile, after multivariable adjustment. Elevated serum UA levels were still significantly associated with most individual components of MS, the multiple adjusted OR was 3.29 (95% CI: 2.71, 3.98) for high BMI, 3.54 (95% CI: 2.93, 4.27) for hypertension, 2.49 (95% CI: 1.98, 3.14) for dyslipidemia, comparing subjects in the highest quartile with those in the lowest quartile of serum UA concentration. However, no significant association was found between serum UA and hyperglycemia.

Table 5 shows subgroup analysis for the association between serum UA concentration and MS. Odds ratio of MS was found positively associated with serum UA concentration in both male and female subgroups, and a significant interaction was observed between gender and UA concentration (p=0.05). No significant interaction was found between age (<50 or ≥50) and UA concentration for MS, while a significant association between MS and serum UA concentration existed in both subgroups. When investigating the association between serum UA concentration and MS components in subgroups, a significant
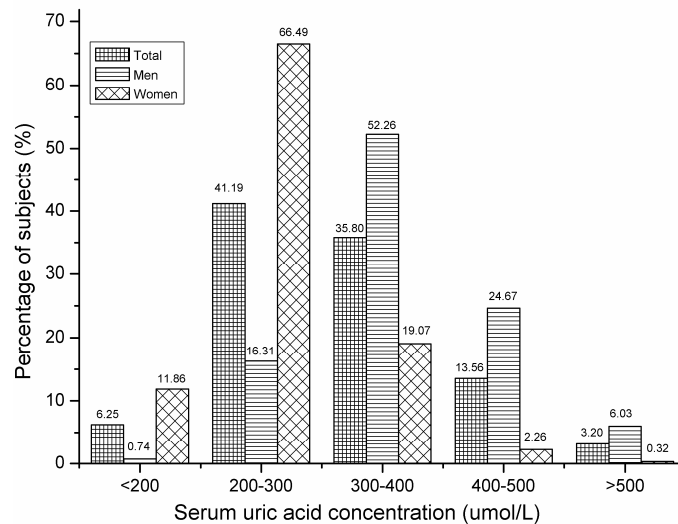
Figure 2. Distributions of serum uric acid concentration among 5,628 subjects. Hyperuricemia is defined by cut-off values of >420 µmol/L for men and >360 µmol/L for women.
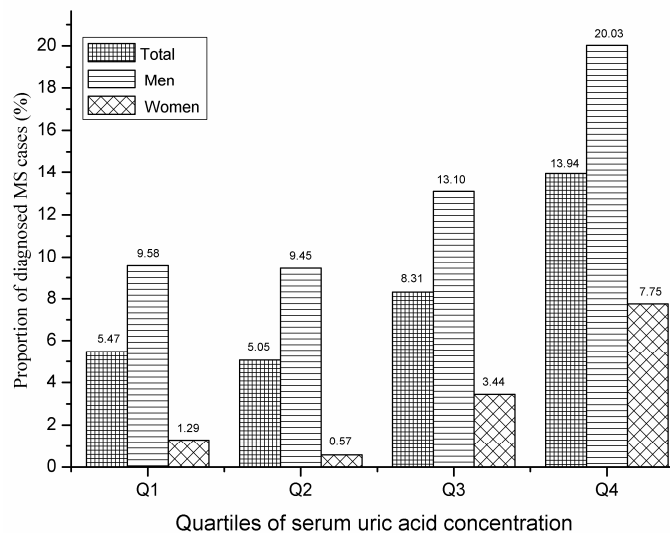

Figure 3. Proportion of diagnosed MS cases by quartiles of serum uric acid concentration among 5,628 subjects. The quartiles of serum uric acid concentration were calculated sex-specifically. In men, the cutoff values of serum uric acid concentration are <320, 320-363, 364-413, and >413 µmol/L respectively; in women, the cutoff values are <224, 224.2-255, 226-294, and >294 µmol/L respectively.

interaction was observed between gender and UA concentration for hyperglycemia, but not for other components such as high BMI, dyslipidemia and hypertension. No significant interaction between age and UA concentration was found for any components of MS, and subjects in the highest quartile of UA concentration had significantly higher odds ratios of MS components compared with those in the lowest quartile regardless of age (<50 or ≥50) (Table 5).

DISCUSSION
In the present study, 22.9% of included men and 5.7% of included women were diagnosed with hyperuricemia, which was very similar to the results of our previous study on Hangzhou population.[21] For men, hyperuricemia prevalence in Thai population was 18.4%,[22] in Beijing urban population and Beijing rural population it was 15.4%.[23] While in women, the hyperuricemia prevalence was 7.8% in Thai population,[22] 11.0% in Beijing urban population and 8.4% in rural population.[23] The regional

variations in hyperuricemia prevalence are likely to be due to differences in dietary habits, such as purines-rich and fructose-rich foods consumption. Purines are precursors of UA, and Fructose metabolisms are reported to increase uric acid levels.[24] For the higher likelihood of hyperuricemia observed in men, this phenomenon is also very common in other populations as reported previously.[25,26] The higher renal clearance of urate and lower tubular urate postsecretory reabsorption of women were thought to be related.

With regard to the proportion of MS cases in the present study, large differences were found between gender subgroups (13.0% in men versus 3.3% in women). But quite remarkably, bias might be introduced by different age structures between subgroups. Nevertheless, the different prevalence between men and women has also been widely reported in other cities, such as Beijing population (15.7% in men versus 10.2% in women) and a Taiwan population study (20.4% in men versus 15.3% in women).[27,28] Furthermore, the higher prevalence of MS among

Table 3. Crude odds ratios and 95% confidence intervals for metabolic syndrome by status of confounding factors

Sample size	MS	High BMI	Hypertension	Dyslipidemia	Hyperglycemia
Hemoglobin					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	2.66 (1.53, 4.62)	1.78 (1.15, 2.74)	3.48 (2.23, 5.41)	3.19 (2.05, 4.95)	1.85 (0.92, 3.73)
Urea nitrogen					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	1.38 (0.59-3.23)	1.02 (0.58-1.81)	0.77 (0.42, 1.40)	1.76 (0.97-3.20)	4.43 (2.32-8.49)
Creatinine					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	4.53 (1.75, 11.73)	4.59 (1.85, 11.40)	4.14 (1.67, 10.26)	3.52 (1.48, 8.39)	4.89 (1.78, 13.4)
White blood cells count					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	2.82 (1.62, 4.92)	2.76 (1.78, 4.29)	2.61 (1.68, 4.06)	1.87 (1.15, 3.05)	2.21 (1.13, 4.33)
Red blood cell count					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	2.02 (1.37, 2.98)	2.19 (1.67, 2.88)	2.04 (1.55, 2.68)	1.80 (1.33, 2.45)	1.16 (0.68, 1.98）
Platelet count					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	0.85 (0.37, 1.96)	1.32 (0.84, 2.05)	1.31 (0.84, 2.03)	1.26 (0.75, 2.13)	0.76 (0.28, 2.09)
Age					
<50 (referent)	1.00	1.00	1.00	1.00	1.00
≥50	2.41 (1.99, 2.92)	1.71 (1.52, 1.93)	1.34 (1.19, 1.51)	4.40 (3.81, 5.08)	3.33 (2.66, 4.15)
Gender					
Women (referent)	1.00	1.00	1.00	1.00	1.00
Men	4.45 (3.51, 5.63)	3.66 (3.24, 4.14)	3.72 (3.30, 4.20)	2.51 (2.17, 2.90)	2.36 (1.87, 3.00)

Table 4. Multivariable adjusted[†] odds ratios and 95% confidence intervals for metabolic syndrome by quartiles of uric acid concentration

	Quartiles of uric acid concentration				p for trend
	Q_1	Q_2	Q_3	Q_4	
High BMI					
Multivariable OR	1.00	1.37 (1.13-1.66)	2.14 (1.77-2.58)	3.29 (2.71-3.98)	<0.01
Hypertension					
Multivariable OR	1.00	1.41 (1.17-1.70)	1.91 (1.59-2.30)	3.54 (2.93-4.27)	<0.01
Dyslipidemia					
Multivariable OR	1.00	1.17 (0.92-1.50)	1.88 (1.49-2.36)	2.49 (1.98-3.14)	<0.01
Hyperglycemia					
Multivariable OR	1.00	0.92 (0.66-1.29)	0.82 (0.59-1.16)	1.21 (0.87-1.67)	0.11
Metabolic syndrome					
Multivariable OR	1.00	0.96 (0.68-1.36)	1.68 (1.22-2.30)	2.84 (2.09-3.86)	<0.01

[†]Multivariable model adjusted for age (continuous), gender (male/female), concentration of hemoglobin (continuous), red blood cells count (continuous), white blood count (continuous) and creatinine (continuous).

men than women was also reported in prospective follow-up study.[29] However, a recently published study which investigated the MS prevalence among people in another region of China (Shiyan City),[19] showed higher prevalence of MS among women than men (37.8% versus 22.9%). The difference might partly due to their study only including subjects older than 50 years and all included subjects were retired employees from the same company, which reduced the representativeness of this study. Overall, the variation of prevalence of MS between men and women has been widely reported and different sex hormone levels between gender subgroups might help explain the discrepancy as reported by Mehmet Agirbasli.[30] In addition, Perez-Torres' study indicated that estrogens were protective against development of cardiovascular diseases in humans and experimental models, but androgens might have an opposite effect.[31] Therefore, androgen/estrogen balance might be also involved in the metabolic pathways associated with MS.

The findings of the logistic regression analysis showed that individuals with elevated serum UA levels had significantly increased likelihood of having MS, independent of their age and gender. These findings were in accordance with previous cross-sectional and prospective studies.[32,33] For the components of MS, significantly positive associations were found between serum UA and high BMI, hypertension and dyslipidemia, which were in accord with results from another population in China.[19] However, there was no significant association between serum UA and hyperglycemia prevalence after multiple adjustments. The findings that glucose competitively inhibited UA reabsorption and enhanced its excretion at the same anatomical position in the gut and that serum UA reduced after the onset of diabetes,[34-36] may also help explain the lack of a positive association between serum UA concentration and diabetes risk in the present population. However, even though the present study supports that people with lower serum UA concentrations are much

Table 5. Odds ratios and 95% confidence intervals for metabolic syndrome by quartiles of uric acid concentration in subgroup analysis

Population subgroup	Quartiles of serum uric acid (μmol/L)				*p* for interaction
	Q_1	Q_2	Q_3	Q_4	
Metabolic syndrome					
Gender					
Men	1.00	1.04 (0.72-1.50)	1.59 (1.12-2.25)	2.57 (1.83-3.62)	0.05
Women	1.00	0.43 (0.13-1.43)	1.99 (0.90-4.43)	3.49 (1.62-7.50)	
Age (y)					
<50	1.00	0.77 (0.47-1.25)	1.50 (0.97-2.32)	2.65 (1.74-4.02)	0.80
≥50	1.00	1.02 (0.62-1.67)	1.53 (0.97-2.40)	2.33 (1.50-3.63)	
High BMI					
Gender					0.24
Men	1.00	1.40 (1.11-1.76)	1.94 (1.54-2.44)	2.93 (2.31-3.72)	
Women	1.00	1.23 (0.85-1.78)	2.35 (1.68-3.30)	3.59 (2.56-5.03)	
Age (y)					0.51
<50	1.00	1.21 (0.95-1.54)	1.99 (1.58-2.52)	3.24 (2.55-4.11)	
≥50	1.00	1.47 (1.07-2.03)	1.93 (1.41-2.64)	2.62 (1.90-3.61)	
Hypertension					
Gender					
Men	1.00	1.41 (1.12-1.76)	1.91 (1.52-2.40)	3.45 (2.72-4.38)	0.98
Women	1.00	1.38 (0.99-1.92)	1.84 (1.33-2.53)	3.51 (2.56-4.80)	
Age (y)					
<50	1.00	1.44 (1.15-1.80)	1.86 (1.48-2.33)	3.66 (2.90-4.61)	0.77
≥50	1.00	1.17 (0.85-1.63)	1.74 (1.27-2.38)	2.79 (2.02-3.86)	
Dyslipidemia					
Gender					
Men	1.00	1.17 (0.89-1.55)	1.71 (1.30-2.25)	2.57 (1.95-3.39)	0.43
Women	1.00	1.13 (0.70-1.82)	2.07 (1.35-3.17)	2.06 (1.33-3.17)	
Age (y)					
<50	1.00	0.97 (0.69-1.38)	1.70 (1.22-2.35)	2.52 (1.82-3.48)	0.51
≥50	1.00	1.13 (0.82-1.56)	1.56 (1.15-2.12)	1.79 (1.31-2.45)	
Hyperglycemia					
Gender					
Men	1.00	0.97 (0.66-1.41)	0.80 (0.54-1.19)	0.99 (0.67-1.48)	0.02
Women	1.00	0.74 (0.36-1.52)	0.84 (0.43-1.63)	1.52 (0.82-2.80)	
Age (y)					
<50	1.00	0.82 (0.50-1.35)	0.89 (0.54-1.46)	1.25 (0.77-2.02)	0.76
≥50	1.00	0.88 (0.56-1.38)	0.65 (0.41-1.03)	1.01 (0.65-1.56)	

The quartiles of serum uric acid concentration were calculated sex-specifically. In men, the cutoff values of serum uric acid concentration are <320, 320-363, 364-413, and >413 μmol/L respectively; in women, the cutoff values are <224, 224.2-255, 226-294, and >294 μmol/L respectively.

less likely to develop MS, one recent study indicated that low serum UA concentrations (<300 μmol/L) were associated with excess all-cause and cardiovascular mortality.[37] Moreover, in the present population, more than 75% of women have UA concentration less than 300 μmol/L, therefore further studies are needed to investigate the all-cause and cardiovascular mortality of central China population stratified by serum UA concentration and gender.

Limitations of this study must be considered. Firstly, the cross-sectional study design could not determine causal roles of serum UA on development of MS. Secondly, even though the age ranges of included subjects were wide, all subjects were restricted to only one area in central China, which might introduce selection bias. Thirdly, the sample size was also relatively limited. Nevertheless, comparison between the present study with others that based on population in other cities of China or other Asian countries were made to show an overall picture.

Conclusion
A significantly positive association between serum UA

level and odd ratio of MS was observed in the present sample of Wuhan population. More prospective studies are needed to verify the association, especially to clarify the mechanisms involved.

REFERENCES
1. He Y, Jiang B, Wang J, Feng K, Chang Q, Fan L, Li X, Hu FB. Prevalence of the metabolic syndrome and its relation to cardiovascular disease in elderly Chinese population. J Am Coll Cardiol. 2006;47:1588-94. doi: 10.1016/j.jacc.2005.11.

074.

2. Gu D, Reynolds K, Wu X, Chen J, Duan X, Reynolds RF, Whelton PK, He J. Prevalence of the metabolic syndrome and overweight among adults in china. Lancet. 2005;365: 1398-405. doi: 10.1016/S0140-6736(05)66375-1.

3. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. Diabetes Care. 2004;27:2444-9. doi: 10.2337/diacare.27.10.2444.

4. Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, Taskinen MR, Groop L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care. 2001;24:683-9. doi: 10.2337/diacare.24.4.683.

5. Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. Am J Med. 2006; 119:812-9. doi: 10.1016/j.amjmed.2006.02.031.

6. Ford ES, Schulze MB, Pischon T, Bergmann, M, Joost HG, Boeing H. Metabolic syndrome and risk of incident diabetes: findings from the European prospective investigation into cancer and nutrition-potsdam study. Cardiovasc Diabetol. 2008;7:35. doi: 10.1186/1475-2840-7-35.

7. Esposito K, Chiodini P, Colao A, Lenzi A, Giugliano D. Metabolic syndrome and risk of cancer: a systematic review and meta-analysis. Diabetes Care. 2012;35:2402-11. doi: 10. 2337/dc12-0336.

8. Zhou J, Zhang Q, Yuan X, Wang J, Li C, Sheng H, Qu S, Li H. Association between metabolic syndrome and osteoporosis: a meta-analysis. Bone. 2013;57:30-5. doi: 10.1016/j. bone.2013.07.013.

9. Qin L, Yang Z, Gu H, Lu S, Shi Q, Xing Y et al. Association between serum uric acid levels and cardiovascular disease in middle-aged and elderly Chinese individuals. BMC Cardiovasc Disord. 2014;14:26. doi: 10.1186/1471-2261-14-26.

10. Fenech G, Rajzbaum G, Mazighi M, Blacher J. Serum uric acid and cardiovascular risk: state of the art and perspectives. Joint Bone Spine. 2014;81:392-7. doi: 10.1016/j.jbspin. 2014.01.008.

11. Lehto S, Niskanen L, Rönnemaa T, Laakso M. Serum uric acid is a strong predictor of stroke in patients with non-insulin-dependent diabetes. Stroke. 1998;29:635-9. doi: 10. 1161/01.STR.29.3.635.

12. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and risk of stroke: a systematic review and meta-analysis. Arthritis Rheumatism. 2009;61: 885-92. doi: 10.1002/art.24612.

13. Fini MA, Elias A, Johnson RJ, Wright RM. Contribution of uric acid to cancer risk, recurrence, and mortality. Clin Transl Med. 2012;1:16. doi: 10.1186/2001-1326-1-16.

14. Timóteo AT, Lousinha A, Labandeiro J, Miranda F, Papoila AL, Oliveira JA, Ferreira ML, Ferreira RC. Serum uric acid: a forgotten prognostic marker in acute coronary syndromes? Eur Heart J Acute Cardiovasc Care. 2013;2:44-52. doi: 10. 1177/2048872612474921.

15. Sundström J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. Hypertension. 2005;45:28-33. doi: 10.1161/01.HYP.0000150784. 92944.9a.

16. Nan H, Dong Y, Gao W, Tuomilehto J, Qiao Q. Diabetes associated with a low serum uric acid level in a general Chinese population. Diabetes Res Clin Pract. 2007;76:68-74. doi: 10.1016/j.diabres.2006.07.022.

17. Ogura T, Matsuura K, Matsumoto Y, Mimura Y, Kishida M, Otsuka F, Tobe K. Recent trend of hyperuricemia and obesity in Japanese male adolescents, 1991 through 2002. Metabolism. 2004;53:448-53. doi: 10.1016/j.metabol.2003.11.017.

18. Milionis HJ, Kakafika AI, Tsouli SG, Athyros VG, Bairaktari ET, Seferiadis KI, Elisaf MS. Effects of statin treatment on uric acid homeostasis in patients with primary hyperlipidemia. Am Heart J. 2004;148:635-40. doi: 10. 1016/j.ahj.2004.04.005.

19. Dai X, Yuan J, Yao P, Yang B, Gui L, Zhang X et al. Association between serum uric acid and the metabolic syndrome among a middle- and old-age Chinese population. Eur J Epidemiol. 2013;28:669-76. doi: 10.1007/s10654-013-9829-4.

20. Expert panel on metabolic syndrome of Chinese diabetes society. Recommendations on metabolic syndrome of Chinese diabetes society. Chinese Journal of Diabetes. 2004;12: 156-61. (In Chinese)

21. Cai Z, Xu X, Wu X, Zhou C, Li D. Hyperuricemia and the metabolic syndrome in Hangzhou. Asia Pac J Clin Nutr. 2009;18:81-7.

22. Lohsoonthorn V, Dhanamun B, Williams MA. Prevalence of hyperuriceamia and its relationship with metabolic syndrome in Thai adults receiving annual health exams. Arch Med Res. 2006;37:883-9. doi: 10.1016/j.arcmed.2006.03.00 8.

23. Li Y, Stamler J, Xiao Z, Folsom A, Tao S, Zhang H. Serum uric acid and its correlates in Chinese adult populations, urban and rural, of Beijing. The PRC-USA Collaborative Study in Cardiovascular and Cardiopulmonary Epidemiology. Int J Epidemiol. 1997;26:288-96. doi: 10.1093/ije/26.2. 288.

24. Dornas WC, de Lima WG, Pedrosa ML, Silva ME. Health implications of high-fructose intake and current research. Adv Nutr. 2015;6:729-37. doi: 10.3945/an.114.008144.

25. Sui X, Church TS, Meriwether RA, Lobelo F, Blair SN. Uric acid and the development of metabolic syndrome in women and men. Metabolism. 2008;57:845-52. doi: 10. 1016/j.metabol.2008.01.030.

26. Conen D, Wietlisbach V, Bovet P, Shamlaye C, Riesen W, Paccaud F, Burnier M. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. BMC Public Health. 2004;4:9-17. doi: 10.1186/1471-2458-4-9.

27. Li ZY, Xu GB, Xia TA. Prevalence rate of metabolic syndrome and dyslipidemia in a large professional population in Beijing. Atherosclerosis. 2006;184:188-92. doi: 10.1016/j. atherosclerosis.2005.03.033.

28. Yang FY, Wahlqvist ML, Lee MS. Body mass index (BMI) as a major factor in the incidence of the metabolic syndrome and its constituents in unaffected Taiwanese from 1998 to 2002. Asia Pac J Clin Nutr. 2008;17:339-51.

29. Hadaegh F, Hasheminia M, Lotfaliany M, Mohebi R, Azizi F, Tohidi M. Incidence of metabolic syndrome over 9 years follow-up; the importance of sex difference in the role of insulin resistance and other risk factors. Plos One. 2013;8: e76304. doi: 10.1371/journal.pone.0076304.

30. Agirbasli M, Agaoglu NB, Orak N, Caglioz H, Ocek T, Poci N, Salaj A, Maya S. Sex hormones and metabolic syndrome in children and adolescents. Metabolism. 2009;58:1256-62. doi: 10.1016/j.metabol.2009.03.024.

31. Pérez-Torres I, Guarner V, EI Hafidi M, Baños G. Sex hormones, metabolic syndrome and kidney. Curr Top Med Chem. 2011;11:1694-705. doi: 10.2174/1568026117961175 77.

32. Chiou WK, Wang MH, Huang DH, Chiu HT, Lee YJ, Lin JD.The relationship between serum uric acid level and metabolic syndrome: difference by sex and age in Taiwanese. J Epidemiol. 2010; 20:219-24. doi: 10.2188/jea.JE20090078.

33. Zhang Q, Zhang C, Song X, Lin H, Zhang D, Meng W et al. Longitudinal cohort based association study between uric acid level and metabolic syndrome in Han Chinese urban population. BMC Public Health. 2012;12:419. doi: 10.1186/

1471-2458-12-419.

34. Lin KC, Tsai ST, Lin HY, Chou P. Different progressions of hyperglycemia and diabetes among hyperuricemic men women in the Kinmen study. J Rheumatol. 2004;31:1159-65.

35. Herman JB, Goldbourt U. Uric acid and diabetes: observations in a population study. Lancet.1982;31:240-3. doi: 10. 1016/S0140-6736(82)90324-5.

36. Nan H, Qiao Q, Söderberg S, Pitkäniemi J, Zimmet P, Shaw J et al. Serum uric acid and incident diabetes in Mauritian and Creole populations. Diabetes Res Clin Pract. 2008;80: 321-7. doi: 10.1016/j.diabres.2008.01.002.

37. Kuo CF, See LC, Yu KH, Chou IJ, Chiou MJ, Luo SF. Significance of serum uric acid levels on the risk of all-cause and cardiovascular mortality. Rheumatology. 2013;52:127-34. doi: 10.1093/rheumatology/kes223.