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Original Article

Associations of serum uric acid levels with cardiovascular health factors: Differences by sex, age and body mass index in Chinese participants

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ABSTRACT

Background: Recently, the American Heart Association developed a set of 3 ideal cardiovascular (CV) health factors. However, information on whether associations of uric acid (UA) with the CV health factors is influenced by sex, age, and body mass index (BMI) is limited.
Methods: We conducted a cross-sectional analysis using a cohort of 10,420 people aged 20–100 years, who underwent health checkups in 2009. CV health factors were defined as untreated total cholesterol (TC) < 200 mg/dl, untreated systolic/diastolic blood pressure (BP) < 120/80 mm Hg, and untreated fasting plasma glucose (FPG) < 100 mg/dl.
Results: The association of UA with each CV health factor was gender-specific. The interaction terms (gender × UA level) comparing change in prevalence of each CV health factor between the 1st and 4th UA quartiles showed a significantly greater reduction among women (all $P < 0.01$). In addition, the interactions between UA levels and age on prevalence of each CV health factor were statistically significant (all $P < 0.01$). Furthermore, absolute reductions in the prevalence of ideal levels of BP, and TC across ordinal UA quartiles were greater in obese individuals than in overweight and normal-weight individuals (all $P < 0.01$). Finally, UA showed a bell-curved relation with the prevalence of ideal FPG among all BMI categories.
Conclusions: Elevated UA inversely associated with each CV health factor and these associations were influenced by gender, age and BMI. Elevated UA levels should alert clinical suspicion for a potential coexistence of low frequency of CV health factors.

1. Introduction

Although the conclusions as to whether serum uric acid (UA) is an independent risk factor for cardiovascular disease (CVD) have been inconsistent [1–4], increasing evidence suggests that elevated UA level is frequently encountered in individuals with obesity, glucose intolerance, hypertension, and dyslipidemia [5–9]. Recently, the American Heart Association (AHA) released the "Strategic Impact Goal Through 2020 and Beyond"[10], in which the AHA developed a set of 3 ideal cardiovascular (CV) health factors including untreated total cholesterol (TC) < 200 mg/dl, untreated systolic blood pressure (SBP) < 120 mm Hg and diastolic blood pressure (DBP) < 80 mm Hg, and untreated fasting plasma glucose (FPG) < 100 mg/dl, and created 3 states for each of the 3 metrics that reflected poor, intermediate, and ideal health [10]. To the best of our knowledge, information on the associations between UA and the AHA definition of "ideal CV health factors" is scant. In addition, both the UA levels and CV health factors are influenced by sex, age, and body mass index (BMI) [11,12], it also remains to be evaluated whether comparable relationship between UA and the CV health factors has occurred in both genders, across age groups, or BMI categories. The objective of our study was, therefore, (1) to examine the relationships between UA levels and the CV health factors, and (2) to explore whether the relationships between UA levels and the CV health factors are influenced by gender, age, and BMI.

2. Methods

2.1. Subjects

The study participants were Chinese employees and retired workers aged 20–100 years, from the Wuhan Iron and Steel Company (WISCO), which is one of the largest iron and steel companies in China. In WISCO,

Abbreviations: UA, uric acid; CVD, cardiovascular disease; AHA, American Heart Association; TC, total cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; BMI, body mass index.

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the Industrial Safety and Health Law requires employees and retired workers to receive periodic health examinations at the WISCO General Hospital (Wuhan, China). The present cohort included all employees and retired workers who received a comprehensive health examination in 2009 (n = 11,719). We excluded 1299 participants, comprising 893 participants who were taking medications for hypertension, diabetes, dyslipidemia, or hyperuricemia, 369 missing information on age, sex, weight, height, BP, FPG, TC or UA, and 37 with chronic kidney disease. The remaining available 10,420 participants (6784 men and 3686 women) were included in our data analysis. The fact that men accounted for 65.1% of total participants was in consistent with the proportion of male employees at WISCO. According to the Private Information Protection Law, information that might identify subjects was safeguarded by the Health Examination Center. This study was approved by the institutional review board of WISCO general Hospital. Because we only retrospectively accessed a de-identified database for purposes of analysis, informed consent requirement was exempted by the institutional review board.

2.2. Demographic characteristics

Information on age, sex, histories of current and previous illness, and medical treatment were surveyed by structured questionnaires. Participants were stratified by age into 6 subgroups: 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, and ≥70 years.

2.3. Biochemical measurements

Weight was measured with the participants wearing light clothing and height was measured without shoes. BMI was calculated as weight (in kilograms) divided by the square of height (in meters). Participants' seated blood pressure was measured twice for every 5 min on the right arm after 5 min of rest by trained nurses with a sphygmomanometer. The mean of the two readings was used in data analysis. All physical examinations were performed by the same manner.

Overnight fasting (at least 8 h) blood samples were collected from the antecubital vein of each individual. Serum levels of UA, FPG, and TC were determined on an autoanalyzer (Hitachi 7600, Ltd, Tokyo, Japan). UA was measured using a colorimetric enzymatic method. FPG concentration was measured by glucose oxidase method. TC was analyzed by standardized enzymatic method. All the blood measurements followed the same protocol.

2.4. Definitions

According to the AHA definition [10], we outlined the CV health factors and the 3 levels (poor, intermediate, or ideal) of each CV factor in Table 1. Normal weight, overweight, and obesity were defined according to the World Health Organization classification (normal weight: BMI 18.5–24.9 kg/m^2; overweight: BMI 25–29.9 kg/m^2; obesity: BMI ≥30 kg/m^2) [13].

Table 1
Definition of poor, intermediate, and ideal cardiovascular health for each cardiovascular health factor for adults aged ≥20 years.
Adapted from Loyd-Jones et al. [10].

	Poor	Intermediate	Ideal
Blood pressure, mm Hg	SBP ≥ 140 or DBP ≥ 90	SBP 120–139 and DBP 80–89	<120/80
Total cholesterol, mg/dl	≥240	200–239	<200
Fasting plasma glucose, mg/dl	≥126	100–125	<100

Notes: SBP = systolic blood pressure; DBP = diastolic blood pressure.

2.5. Statistical analysis

All statistical analyses were conducted using SPSS software (version 12.0 for windows; SPSS, Chicago, IL, USA). Given that UA levels are substantially different between men and women, sex specific quartiles of UA levels were established (quartile ranges of UA (mg/dl) in men/women: 1st: ≤4.9/3.6 mg/dl, 2nd: 5.0-5.6/3.7–4.2 mg/dl, 3rd: 5.7–6.4/4.3–4.9 mg/dl, and 4th: ≥6.5/5.0 mg/dl). Continuous and categorical variables were presented as mean ± SD and percentages, respectively. One-way ANOVA was applied to compare differences in means between groups. Trends in prevalence of each CV health factor across ordinal UA quartiles were assessed by Cochran–Armitage trend testing. To assess if changes in the prevalence of CV health factors throughout the ordinal UA quartiles and between the first and the fourth UA quartiles differed by BMI group, logistic regression analysis was utilized to examine potential interaction effects between UA levels and BMI categories. The process was repeated separately for age and sex groups. A two-tailed P value of <0.05 was considered to be significant.

3. Results

3.1. Characteristics of the study participants

The clinical characteristics of the participants were showed in Table 2. We found no significant differences in FPG between men and women. Women were older and had lower values of BMI, systolic/diastolic BP, and UA, and higher levels of TC than did men (all P < 0.01).

3.2. Prevalence of CV health factors by quartiles of UA concentration

Both men and women in the highest UA quartile exhibited the lowest prevalence of ideal levels of BP, TC, and FPG (Table 3). Men had lower prevalence of ideal BP and higher prevalence of ideal TC than did women at a given quartile of UA. For the 1st and 2nd UA quartiles, men had lower prevalence of ideal FPG compared with women. For the 3rd and 4th UA quartiles, women had a lower prevalence of ideal FPG compared with men. Ideal levels of BP were the least frequent of ideal CV health factor across all groups, particularly in participants with the highest UA quartile, in whom fewer than one third were in the ideal ranges.

3.3. Interaction effect between UA levels and sex on the prevalence of CV health factors

The downward trends in the prevalence of ideal levels of BP, and TC with increasing UA levels persisted in both sexes. The prevalence of ideal FPG remained stable across UA quartiles among men. In comparison, the prevalence of ideal FPG decreased linearly with increasing UA levels among women (Table 4). The interaction terms (gender × UA levels) comparing change in prevalence of each CV health factor between the 1st and the 4th UA quartiles showed significantly greater reductions in prevalence of each CV health factor among women (all P < 0.001).

Table 2
Clinical characteristics of participants.

	Men, n = 6734	Women, n = 3686	p
Age (year)	49.3 ± 14.9	51.4 ± 13.7	<0.01
Body mass index (kg/m^2)	24.2 ± 2.8	23.4 ± 3.1	<0.01
Systolic blood pressure (mm Hg)	124.8 ± 16.5	120.3 ± 16.2	<0.01
Diastolic blood pressure (mm Hg)	79.6 ± 11.1	75.6 ± 10.3	<0.01
Total cholesterol (mg/dl)	4.5 ± 0.9	4.8 ± 1.0	<0.01
Fasting plasma glucose (mg/dl)	95.4 ± 23.4	95.4 ± 25.2	0.255
Uric acid (mg/dl)	5.7 ± 1.2	4.3 ± 1.1	<0.01

Data are presented as means and standard deviations.