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Research paper

Higher uric acid is associated with higher rate of metabolic syndrome in Chinese elderly

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ABSTRACT

Background: Although uric acid (UA) is not in the definition of metabolic syndrome (MetS), several studies had shown the positive correlation between UA and MetS. Due to the progress in the public health, the aging of the general population becomes a major issue. However, the aforementioned relationship between UA and MetS is not fully explored in elderly group. To fill up this deficient piece of knowledge, we enrolled Chinese elderly to shed light on the relationships between UA levels and MetS.
Methods: We randomly selected subjects aged 65 and older undergoing routine health checkups in Taiwan. After excluding subjects with taking medications known to affect components of MetS or UA, a total of 27,553 Chinese were eligible for analysis. All the participants were further divided into four groups according to the UA level.
Results: All the MetS components were significantly lower in the UA1 group. In simple correlation, all the MetS components were also correlated with UA. However, age and blood pressure became non-significant in multiple regressions. Compared to UA1, all the other 3 groups had higher odds ratio for MetS.
Conclusion: Higher UA level have higher rate of having MetS in Chinese elderly. UA could be regard as an ancillary tool for the awareness of MetS.

1. Introduction

The clustering of dyslipidemia, obesity, hypertension and hyperglycemia has been recognized first by Reaven et al. since 1988 [1] and it was found to be highly correlated with developing cardiovascular diseases (CVD) and diabetes. Later, it was termed formerly as metabolic syndrome (MetS). In recent two decades, the prevalence of obesity has been increasing in an alarming rate [2]. In company with the obesity, the CVD and diabetes have become the one of the most common causes of death in many countries. In order to early detect subjects with high risks for these two diseases, the National Cholesterol Education Program Adult Treatment Panel III have defined the diagnostic criteria of MetS [3]. After these definitions, large numbers of papers have been published to evaluate the roles of MetS from different aspects.

Uric acid (UA) is the by-product of purine metabolism generated during the breakdown of nucleic acids. Although UA is not included in the definition of the MetS, there were evidences showed that increased UA level is related to the worsening insulin resistance and the development of hypertension [4]. In addition, Ishizaka et al. [5] also found that UA is independently correlated with waist circumference (WC), which is another core factor in MetS. Based on these observations, numbers of studies have shown the positive correlations between UA and MetS [6,7].

Due to the progress in the public health, the aging of the general population becomes a major issue in many developed countries. Therefore, how to early detect subjects at risks for CVD is main task for both health providers and health department of government. Under these circumstances, the role of UA becomes more important, especially in the elderly. However, to our knowledge,

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the aforementioned relationship between UA and MetS is not fully explored in this age group. To fill up this deficient piece of knowledge, we enrolled 27,553 Chinese elderly to shed light on the relationships between UA levels and MetS.

2. Method

2.1. Study population

The data were collected from the MJ Health Screening Centers' database in Taiwan from 1999 to 2008. MJ Health Screening Centers are a privately owned chain clinics located throughout Taiwan that provides regular health examinations to their members. All study participants were anonymous, and informed consents were obtained from all participants. Data were provided by MJ Health Screening Center for research purposes only, and the study protocol was approved by the institutional review board of MJ Health Screening Center.

We randomly selected aged 65 and older undergoing routine health checkups at the MJ Health Screening Centers in Taiwan. Among them, 15,832 men and 14,359 women were healthy in the last year annually healthy checkup. They did not have any past history of major diseases of myocardial infarction, angina, stroke, peripheral arterial occlusion disease, type 2 diabetes, hypertension and dyslipidemia. Then we excluded 227 male subjects and 274 female subjects with taking medications known to affect components of MetS or UA in the current status. These medications included antihypertensive drugs of α- and β-blockers, diuretics, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, calcium channel blockers, oral hypoglycemic agents, insulin, lipid lowering agents of statin and fibrate, and uric acid lowering agents of allopurinol, etc. However, subjects with newly diagnosed hypertension, type 2 diabetes or dyslipidemia without medication were included in the current study. Another 2137 subjects were further excluded due to the missing data of MetS components or UA level. At last, a total of 14,442 men and 13,111 women were eligible for analysis. All the participants were further divided into four groups according to the UA level (UA1 to UA 3, from lowest to highest tertile in normal range of UA, and hyperuricemia groups of > 6.8 mg/dl in male and > 6.0 mg/dl in female).

2.2. Anthropometrics measurements and general data

Questionnaires were provided by senior nurses to obtain the medical history and current medications. Complete physical examinations were then performed. Body weight and height were measured by an auto-anthropometer, Nakamura KN-5000A (Nakamura, Tokyo, Japan). Body weight was measured to the nearest 0.1 kg with subjects' barefoot and wearing light indoor clothing. Body height was recorded to the nearest 0.1 cm. Body mass index was calculated as weight in kilograms divided by the square of height in meters. WC was taken at the midway point between the inferior margin of the last rib and the crest of the ileum in a horizontal plane and measured to the nearest 0.1 cm. Blood pressure was measured twice, on the right arm, with the subject in a sitting position, after 5 min of rest, using a computerized auto-mercury-sphygmomanometer, Citizen CH-5000 (Citizen, Tokyo, Japan). Two measurements were taken at 10 min intervals. The mean of these two readings was used in analysis.

2.3. Laboratory measurements

After the subject fasted for 10 hours, blood samples were drawn from the antecubital vein for biochemical analysis. Plasma was separated from blood within 1 hour and stored at -30 °C and analyzed for fasting plasma glucose (FPG) and lipid profiles. The FPG was detected using a glucose oxidase method (YSI 203 glucose analyzer, Scientific Division, Yellow Springs Instruments, Yellow Springs, OH). Total cholesterol and triglycerides (TG) were measured using the dry, multilayer analytical slide method in the Fuji Dri-Chem 3000 analyzer (Fuji Photo Film, Minato-Ku, Tokyo, Japan). Serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) concentration were analyzed using an enzymatic cholesterol assay following dextran sulfate precipitation. Serum UA was measured by uricase-peroxidase method, Abbott C8000 analyzer (Abbott Laboratories, Abbott Park, IL, USA).

2.4. Definition of metabolic syndrome

In the current study, MetS was regarded as a risk factor for future CVD/diabetes and thus the occurrence of MetS was the primary endpoint. We used the following modified Adult Treatment Panel III [3] and International Diabetes Federation [8] criteria to define MetS:

- WC $\geq$ 90 cm and 80 cm for Taiwanese male and female, respectively;
- Systolic blood pressure (SBP) $\geq$ 130 mmHg or diastolic blood pressure (DBP) $\geq$ 85 mmHg;
- TG $\geq$ 150 mg/dL;
- HDL-C $<$ 40 mg/dL in male and $<$ 50 mg/dL in female;
- FPG $\geq$ 100 mg/dL.

Having more than three of these components was diagnosed as MetS.

2.5. Statistical analysis

The data are presented as the means $\pm$ standard deviation unless indicated otherwise. The one-way ANOVA test using the Bonferroni test as a post-hoc test was applied to determine differences in continuous variables between the tertile groups. Correlations between UA and each metabolic risk factor were evaluated using the Pearson correlation. Multivariate stepwise regression analysis was further applied to investigate which of the significant MetS components were truly independent risk factors for UA. Logistic regression analysis was used to calculate odds ratios (ORs) for having MetS. In the same time, a level of UA would be identified as the suggested "critical level" to have MetS by receiver operating characteristic (ROC) curves. A P-value (two-sided) < 0.05 was considered to be significant. All statistical analyses were performed using PASW Statistics 18.0 software (SPSS inc., Chicago, IL).

3. Result

Among the 27,553 subjects, 3791 male and 4658 female participants had MetS. The anthropometric variables of blood pressure, plasma biochemistries in subjects with and without MetS were shown in Table 1 (MetS+, MetS−, respectively). All the parameters except total cholesterol were significantly different in these two groups. In particular, UA was higher in MetS+ group. The relationship between incidence of MetS and UA is shown in Fig. 1. Significant positive correlation could be noted ($P < 0.001$ in both genders). The study subjects were then divided into quartiles according UA level. Table 2 showed the comparisons of the demographic and biochemistry data in the four groups of UA1 to UA3 and hyperuricemia group. All the parameters were significantly lower in the UA1 group. When simple correlation was used to further examine their relationships, not surprisingly, they were