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Prospective study of serum uric acid levels and incident metabolic syndrome in a Korean rural cohort

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ABSTRACT

Objective: Recent studies have demonstrated an association between serum uric acid (SUA) levels and metabolic syndrome (MetS). However, paucity of available data regarding the cause and effect relationship between SUA and MetS in healthy adults is still a big challenge which remains to be studied. Therefore, we investigated whether SUA predicts new onset of MetS in a population-based cohort study.
Methods: The study included 1590 adults (661 men and 929 women) aged 40–70 years without MetS at baseline (2005–2008) and subjects were prospectively followed for 2.6 years. To evaluate the relationship between SUA and MetS, we divided the aforementioned subjects into quintiles (SUA-I to SUA-V) from the lowest to the highest values of SUA. SUA was measured by the enzymatic colorimetric method. We used category-free net reclassification improvement (NRI) and integrated discrimination improvement (IDI) to characterize the performance of predicted model.
Results: During a mean of 2.6 years of follow-up, 261(16.4%) adults developed MetS. MetS variables were significantly related to the baseline SUA level. Waist circumference (WC), blood pressure (BP), and serum triglyceride (TG) were significantly higher in the highest quintile of SUA compared to the lowest SUA quintile in men and women. After adjustment for age, total cholesterol and low-density lipoprotein cholesterol (LDL-C) in men and women, subjects in the fifth quintiles of SUA showed significantly higher ORs for incident MetS. The association between hyperuricemia and new onset of MetS were consistently stronger in women than men. Additionally, among women, we found an improvement in the area under the ROC curve in the models that added SUA to core components of MetS.
Conclusion: Our study suggests that SUA is significantly correlated with future risk of WC, BP, TG and may predicted as a risk factor for developing MetS. SUA may have a clinical role in predicting new-onset metabolic syndrome among women. Large prospective study is needed to reveal the clinical significance of SUA in metabolic disease.

1. Introduction

Metabolic syndrome (MetS) is characterized by the grouping of cardiovascular risk factors, including high blood pressure (BP), abdominal obesity, dyslipidemia, and increased glucose concentration [1]. Subjects with MetS are linked with an increased risk of developing type 2 diabetes and cardiovascular disease (CVD) [2,3]. The prevalence of MetS in Korea has been immensely increased from 24.9% in 1998 to 31.3% in 2007 due to rapid lifestyle changes [4].

Apart from the dietary habit and variables of MetS, other factors have also played a significant role in higher prevalence and incidence of developing MetS. Several epidemiological studies have established the link between hyperuricemia and the development of MetS in various populations which may relate to the burden of

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diabetes and CVD [5–9]. Furthermore, studies evaluating a sex-related association between SUA and development of MetS have also been highly intensified [5,10,11].

Recently, the association between serum uric acid (SUA) and MetS was monitored not only in hyperuricemia, but also in the normal range of SUA [12,13]. Nevertheless, very limited information is available about its ability as a predictor of MetS and its components and additional clinical utility in epidemiological perspective. Hence, we designed a follow-up study to prospectively examine the association between SUA and the incidence of MetS and its components as well as the predictive ability of SUA in identifying people who will develop new onset of MetS stratified by sex in Korean rural cohort.

2. Methods

2.1. Study participants

The Korean Genome and Epidemiology Study on Atherosclerosis Risk of Rural Areas in the Korean General Population (KoGES-ARIRANG), a population-based prospective cohort study designed to estimate the prevalence, incidence, and risk factors for chronic degenerative disorders such as diabetes, hypertension, osteoporosis, and cardiovascular disease [14–16]. The adults aged between 40 and 70 years residing in the rural areas of Wonju and Pyeongchang in South Korea participated in the study. The baseline study was executed from November 2005 to January 2008, comprised of 5178 adults (2127 men and 3051women). 3862 (74.6%) subjects were attended during the first follow-up survey (April 2008–January 2011). We then excluded 1020 subjects with MetS at baseline, 1218 subjects without baseline SUA measurement, 20 subjects with a history of cardiovascular disease at baseline and 14 subjects without complete data. In total, 1590 participants were included in the present analysis (661 men and 929 women) (Fig. 1). The study protocol was approved by the institutional review board of Yonsei University College of Medicine. Informed consent was obtained from each participant in the study.

2.2. Data collection and measurements

At study entry, participants completed the medical history and lifestyle questionnaire and went through a standardized health examination according to the optimum procedures. For anthropometrical measurements, body weight and height were measured, with the participants barefooted and wearing light indoor clothing. Waist circumference (WC) was measured using a tape (SECA-200; SECA, Hamburg, Germany) in a horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest. BP was measured with a standard mercury sphygmomanometer (Baumanometer, Copiague, NY) twice on the right arm of the participants. The mean of the two BP readings was used for the data analyses.

Baseline information on current smoking status and alcohol intake was collected by self-reported questionnaire. Subjects who answered “yes” to the question “Do you perform physical exercise regularly enough to make you sweat?” were designated as the regular exercise group.

Venous blood samples were collected from all participants after fasting for >12 h or overnight. Fasting blood glucose (FBG) was measured by a glucose oxidase–based assay. Serum concentrations of high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) were determined by enzymatic methods (Advia 1650; Siemens, Tarrytown, NY). Low-density lipoprotein (LDL)-cholesterol was calculated using Friedewald's formula: LDL-cholesterol = Total cholesterol − (HDL-C + TG/5).

SUA was measured by the enzymatic colorimetric method. In this method, SUA is oxidized by uricase to allantoin and hydrogen peroxide based on the uricase-peroxidase method. In the following reactions, the oxidative condensation of N-ethyl-N-(2-hydroxy-3-sulfopropyl)-3-methylaniline and 4-aminophenazone produces a red chromogen in the presence of peroxidase and hydrogen peroxide [17]. An automated analyzer was used to measure the intensity of the color produced in the sample and the values were reported in mg/dL.

2.3. Definition of MetS

MetS was defined according to the criteria of the harmonized definition [18] for MetS, which was the end-point of this study at the follow-up visit. This definitions includes the presence of at least three out of five metabolic abnormalities: 1) abdominal obesity, defined as a waist circumference ≥90 cm for men or ≥85 cm for

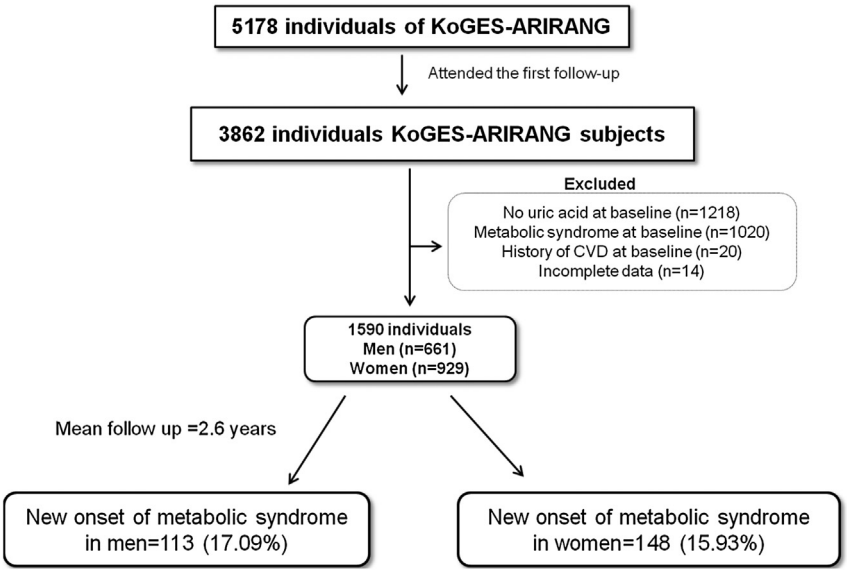

Fig. 1. Descrpition of the study population.