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Central obesity is an independent risk factor for microalbuminuria in both the general Korean women and nondiabetic nonhypertensive subpopulation: Association of microalbuminuria and metabolic syndrome from the Korea National Health and Nutrition Examination Survey 2011–2012

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ABSTRACT

Background: We investigated the major contributing component of metabolic syndrome (MetS) that results in microalbuminuria (MAU) in the general population as well as in nondiabetic nonhypertensive subjects.
Methods: The study population consisted of a total of 9961 subjects (4429 men and 5532 women) who participated in the Korea National Health and Nutrition Examination Surveys conducted in 2011 and 2012. MAU was defined as a urine albumin-to-creatinine ratio of >3.39 mg/mmol. After analyzing the contribution of each five MetS components for the presence of MAU with adjustment for other risk factors in the total population, we further examined the contribution of these components to MAU in the nondiabetic nonhypertensive subpopulation.
Results: The most significantly associated factors for MAU in both genders were high blood pressure, followed by impaired fasting glucose, and high triglycerides. In addition, central obesity contributed significantly to MAU only in women. For the nondiabetic nonhypertensive subpopulation, high blood pressure in both genders and central obesity in women were important risk factors for MAU. We suggest two possible hypotheses for the gender different phenomenon.
Conclusions: Central obesity was an independent risk factor for MAU in the general Korean women as well as in the nondiabetic nonhypertensive women.

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1. Introduction

Metabolic syndrome (MetS) is a constellation of common metabolic disorders that result from impaired glucose tolerance, dyslipidemia, hypertension, and central obesity [1]. The diagnostic criteria for MetS have undergone several updates and changes. The first criteria proposed by the World Health Organization in 1998 included components of diabetes, hypertension, dyslipidemia, obesity, and microalbuminuria (MAU). However, MAU has been excluded from the subsequent diagnostic criteria for MetS, as suggested by the European Group for the Study of Insulin Resistance (1999), National Cholesterol Education Program Third Adult Treatment Panel (2001), American Association of Clinical Endocrinologists (2003), and International Diabetes Federation (2005). Although there have been some suggestions to adjust the MetS criteria based on clinical outcomes and racial variances, MAU was not emphasized as a component of MetS until recently [2]. However, the important association between MAU and MetS has been supported by several recent studies [3,4].

It has been traditionally determined that an increased excretion of albumin alone (>30 mg/day) is a sensitive marker of progressive diabetic glomerulopathy in type I diabetes patients [5]. MAU has also been recognized as an early sign of renal damage and an independent predictor for end-stage renal disease in patients with type I and type II diabetes and also in the general population. More importantly, MAU has been emphasized as an important criterion for the definition of chronic kidney disease (CKD), as suggested by Kidney Disease Improving Global Outcomes (KDIGO) group in 2012 [6]. In the new guideline, MAU was introduced as an equally indispensible component for the definition of CKD with the traditional criterion, estimated glomerular filtration rate (eGFR). This modification was based on the fact that MAU was strongly independently associated with not only cardiovascular complication of CKD [7], but also total mortality of CKD [8], indicating the importance of MAU than ever.

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According to the recent reports on the association between MAU and MetS, high blood pressure and high fasting glucose level were commonly suggested as the major risk factors for MAU [3,4]. However, other metabolic parameters have not been studied well about their levels of contribution for the development of MAU. Especially, only few studies focused on the low risk healthy population without having diabetes or hypertension in searching for the risk factors of MAU [9].

The purpose of this study was to investigate the major contributing components of MetS that result in MAU in the general Korean population as well as in the nondiabetic nonhypertensive subpopulation.

2. Materials and methods

2.1. Study population

Data for this study were derived from the Korea National Health and Nutrition Examination Survey (KNHANES) conducted in 2011–2012. The KNHANES is a cross-sectional and nationally representative survey, which is regularly conducted by the Division of Chronic Disease Surveillance, Korea Centers for Disease Control and Prevention to evaluate the health and nutritional status of non-institutionalized Korean people. Out of a total 16,576 Koreans who participated in the KNHANES 2011–2012, we excluded individuals who were aged < 20 y and pregnant (n = 3883). Afterwards, we excluded individuals whose anthropometric, biochemical, medical history and life-style variables, which were included in this study, were not assessed in the survey (n = 2732). Finally, a total of 9961 subjects (4429 men and 5532 women) were analyzed for this study. Written informed consent was obtained from all participants and the KNHANES was conducted with ethical approval from the Institutional Review Board of Korea Center for Disease Control and Prevention (No: 2011-02CON-06-C, 2012-01EXP-01-2C).

2.2. Anthropometric measurements and biochemical assessments

Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, with participants dressed in light indoor clothing without shoes. The waist circumference was measured at the narrowest point between the lower border of the rib cage and the iliac crest. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in triplicate on the right arm, using a mercury sphygmomanometer (W.A. Baum), after the individual has been in the seated position for at least 5 min of rest. The final BP value was obtained by averaging the second and the third BP measurements. Fasting blood samples collected from each participant from the antecubital veins were processed, refrigerated immediately, and transported in cold storage to the central laboratory (Neodin Medical Institute). All samples were analyzed within 24 h after transportation. Serum levels of glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, blood urea nitrogen (BUN), and creatinine were measured using the Hitachi 7600 automated chemistry analyzer (Hitachi). Urine levels of albumin and creatinine were also measured using the Hitachi 7600 automated chemistry analyzer. Serum and urine creatinine assays were calibrated with lyophilized human serum calibrators (Roche Diagnostics) in which the creatinine concentration has been standardized to isotope dilution-mass spectrometry. GFR was estimated by IDMS-traceable Modification of Diet in Renal Disease Study equation: $175 \times (\text{serum creatinine})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ for women})$ [10].

2.3. Definitions

We adopted the modified Asian criteria of MetS from the American Heart Association/National Heart, Lung, and Blood Institute [11], which defines MetS as the presence of ≥3 of the following: central obesity as waist circumference ≥ 90 cm in men and ≥85 cm in women; SBP ≥ 130 mm Hg, DBP ≥ 85 mm Hg, or undergoing antihypertensive drug treatment; fasting plasma glucose ≥ 5.55 mmol/l or undergoing drug treatment for increased glucose; triglycerides ≥ 1.70 mmol/l; HDL-C < 1.04 mmol/l in men and <1.30 mmol/l in women. It is important to note that a lower waist circumference cut-off point has been adopted for Asian populations compared to that for Western populations [12].

For the classification of nondiabetic nonhypertensive population, we analyzed individuals who did not have diabetes mellitus as well as hypertension, which were defined as follows. Diabetes mellitus was defined on the basis of insulin or oral hypoglycemic agent use or fasting plasma glucose ≥ 6.99 mmol/l. Hypertension was defined as either SBP ≥ 140 mm Hg, DBP ≥ 90 mm Hg, or current antihypertensive medication.

MAU was defined as albumin-to-creatinine ratio > 3.39 mg/mmol (30 mg/g), the most commonly used cut-off value recommended by the American Diabetes Association.

2.4. Statistical methods

Participants' characteristics were compared using independent-sample Student's *t*-tests for continuous variables and chi-square tests for categorical variables. Chi-square tests were performed to compare the prevalence of MAU and to estimate the association between MAU prevalence and MetS scores. Simple and multiple logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for MAU with each MetS components as an independent variable. All data were presented as mean ± standard deviation for continuous variables and frequency percentages for categorical variables. All *P*-values were 2-sided and a $P < 0.05$ was considered statistically significant. All analyses were conducted using the PASW Statistics software (ver. 20.0.0; SPSS Inc.).

3. Results

3.1. Characteristics of the study population

The clinical features of the study population are shown in Table 1. The mean age was higher in the MetS group (59.1 ± 13.4 y) than non-MetS group (48.9 ± 16.0 y), indicating MetS is more prevalent in elderly people. All kinds of personal medical history were statistically significantly higher in MetS group than non-MetS group, with the exception of renal failure which showed higher prevalence (0.6%) in MetS group. Considering the lifestyle variables and anthropometric measurements, all factors showed statistically significant difference between MetS group and non-MetS group as expected, except the fact that drinking proportion was higher in non-MetS group. MetS group had higher urine albumin level (0.045 ± 0.227 g/l) than non-MetS group (0.015 ± 0.075 g/l). Similarly, serum creatinine level was higher in the MetS group (77.02 ± 22.92 mol/l) compared to the non-MetS group (73.34 ± 16.85 mol/l). Additionally, the MetS group showed lower eGFR (86.49 ± 18.01 ml/min/1.73 m^2) than the non-MetS group (93.66 ± 17.25 ml/min/1.73 m^2).

The weighted prevalence of MAU in the general Korean population in 2011–2012 was 6.4%. When we divided the subjects into 6 different age groups by decades, the weighted prevalence of MAU increased gradually with age for both men and women (Supplementary Fig. 1A). For the nondiabetic nonhypertensive subpopulation consisting of 2573 men and 3587 women, the weighted prevalence of MAU was 2.5% and similar pattern was observed (Supplementary Fig. 1B). The weighted prevalence of MetS in the general Korean population in 2011–2012 for men and women was 26.8% and 24.4%, respectively.

3.2. Associations between MAU and MetS components in the total population

A simple logistic regression analysis revealed that all MetS components significantly increased the MAU development (Table 2). High BP

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