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Research paper

Association of adiponectin, ghrelin, and leptin with metabolic syndrome and its metabolic components in Sasang constitutional type

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Mounting evidence indicates a significant relationship between Sasang constitutional types (SCTs) and metabolic syndrome (MetS), and between metabolic hormones and risk of MetS. However, studies have not yet examined whether the impact of metabolic hormones on MetS differs according to SCT. The aim of this study was to investigate whether the association of adiponectin, ghrelin, leptin with MetS and metabolic components is affected by SCTs.
Methods: A total of 2370 subjects (1201 men and 1169 women) who participated in the Korean Genome and Epidemiology Study-Ansan cohort between 2007 and 2008 and completed the health-related questionnaire, anthropometric evaluation, and biochemical measurements were included in the analysis. Each constitutional type was defined using an integrated diagnostic method. Total adiponectin, ghrelin, and leptin levels were determined by enzyme-linked immunosorbent assay or radioimmunoassay.
Results: Tae-eum (TE) type had the highest frequency of MetS (29.9%). In multivariate logistic regression analysis adjusted for possible confounders, adiponectin (OR = 0.88, 95% CI: 0.84–0.92; $P < 0.0001$) and leptin levels (OR = 1.05, 95% CI: 1.01–1.08; $P = 0.015$) were significantly associated with MetS in TE type, whereas only adiponectin levels were significantly associated with MetS in So-yang type (OR = 0.81, 95% CI: 0.73–0.90; $P < 0.0001$). Ghrelin levels were not significantly associated with MetS in all SCTs.
Conclusions: This population-based study showed different association of adiponectin, ghrelin, and leptin with MetS and its components according to SCT.

1. Introduction

Sasang constitutional medicine (SCM) is a traditional Korean medicine developed by Lee Je-Ma (1837–1900), a Korean medical specialist. SCM is based on the fundamental concept that people have different susceptibilities to disease and respond with varying efficacy to drugs due to differences in the functional activities of internal organs [1]. There are four classifications of people based on morphological characteristics, emotions, facial features, and temperaments, called Sasang constitutional types (SCTs): Tae-yang (TY), Tae-eum (TE), So-yang (SY), and So-eum (SE) [1,2].

Metabolic syndrome (MetS) is a condition associated with increased

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risk of developing cardiovascular and metabolic diseases, and it shows an increasing trend worldwide [3]. MetS is defined as a clustering of at least three of the five risk factors of abdominal obesity, elevated blood pressure, high serum triglycerides, low high-density lipoprotein cholesterol, and elevated fasting plasma glucose [4]. Recent studies have reported a significant association between cytokines originating from adipose tissue (adipokines), orexigenic hormones and MetS. Low levels of blood adiponectin are associated with a risk of MetS and obesity, whereas high circulating leptin is related to dysregulated metabolic states such as MetS, insulin resistance, and obesity [5,6]. Regarding orexigenic hormone, ghrelin levels were higher in subjects with MetS. Ghrelin levels are negatively associated with BMI, triglyceride (TG) levels, insulin resistance, and total cholesterol levels [7,8].

Recent studies have reported the association between SCTs and MetS. Population-based studies analyzed data from three cohorts to show that the prevalence of MetS was highest in the TE type (50.8%), and the odds ratio for MetS was 2-fold greater in the TE type compared to the SE type [9]. Although many studies have reported significant associations between adipokines, orexigenic hormones and MetS, there is a lack of research showing the relationship between these factors in SCTs. Thus, we aimed to investigate the association of those hormones with MetS and its components in SCTs using data from a large population-based study in Korea, investigating the influence of SCTs in these associations.

2. Materials and methods

2.1. Study design and population

Data from participants enrolled in the Korean Genome and Epidemiology Study (KoGES)-Ansan cohort, an ongoing population-based cohort, were included for cross-sectional analysis in the present study. In brief, KoGES-Ansan cohort started in 2001 with 5015 participants (2521 men and 2494 women; ages 40–69 years) to identify the epidemiologic characteristics of chronic diseases among Koreans [10]. All participants underwent physical examination, comprehensive health examination, onsite interviews, and laboratory assessment. They were recruited biennially for follow-up assessments after their baseline visit. Of 3255 participants who were enrolled in the cohort between 2007 and 2008 (3rd follow-up period), 2609 individuals completed the questionnaire, anthropometric evaluation, and biochemical measurements. After excluding incomplete data (missing data) and participants with extreme outliers of biochemical data (n = 239), a total of 2370 subjects (1201 men and 1169 women) were included in the analysis. Flowchart of subject selection is shown in Fig. 1. All participants provided written informed consent. The study protocol was approved by the Human Subjects Review Committee at Korea University Ansan Hospital.

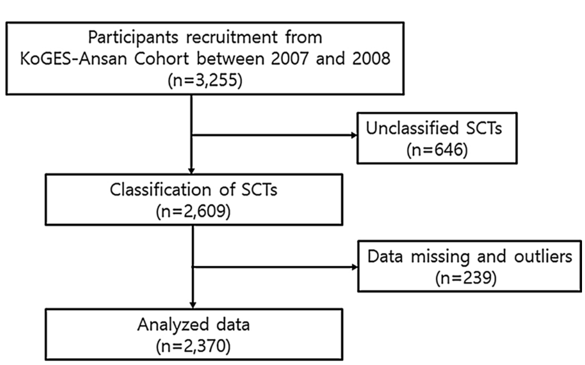

Fig. 1. Flowchart of subject selection for association between metabolic hormones and metabolic syndrome in SCTs.

2.2. Classification of SCTs

Each constitutional type was defined using an integrated diagnostic method [11] that generates probability values for each type by integrating individual quantitative data regarding facial images, voice features, body morphology, and questionnaire responses into a single value. Facial images were taken with a digital camera and processed to extract related variables. The Hidden Markov Model Toolkit program and Praat voice analysis program were used to generate voice variables. Regarding body morphology, the circumference of eight sites, height, and weight were measured and appropriately processed. Questionnaires included information on physiological symptoms, personality, and eating habits.

2.3. Anthropometric and biochemical measurements and definition of metabolic syndrome

Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m^2). Blood pressure (BP) was noninvasively measured in the non-dominant arm in a sitting position with a mercury sphygmomanometer. Degree of physical activity was expressed as metabolic equivalent (MET)-hours/day. Beverage-specific alcohol consumption was calculated in g/day on the basis of the following alcohol content: beer (4.5%), wine (13%), hard liquor (40%), soju (22%), chungju (15%), and makgeoli (6%). Blood samples were acquired from participants who had fasted overnight between 08:30 and 09:30 a.m. for biochemical analyses. Serum total adiponectin levels were determined by enzyme-linked immunosorbent assay (Mesdia Co., Ltd), as previously reported [12]. Both leptin and total ghrelin levels were determined by radioimmuno assay (EMD Millipore, USA), with a sensitivity of 0.437 ng/mL and 93 pg/mL, respectively. Measurements for serum fasting glucose, HDL cholesterol, and TG were accomplished using an authorized commercial laboratory (Seoul Clinical Laboratories, Seoul, Korea) with ADVIA 1650 auto analyzer (Siemens, Tarrytown, NY, USA). In this study, MetS was defined according to the National Cholesterol Education Program Adult Treatment Panel III [13]. When criteria for three or more of the following metabolic components were met, MetS was considered to be present: abdominal obesity, defined as waist circumference ≥90 cm for men and ≥80 cm for women, hypertriglyceridemia (serum triglyceride (TG) ≥150 mg/dl), low high density lipoprotein (HDL) cholesterol (< 40 mg/dl and < 50 mg/ml/dl for men and women, respectively), presence of HTN (systolic/diastolic pressure ≥130/85 mmHg and/or the use of antihypertensive agents), and high fasting blood glucose (≥100 mg/dl or the use of antidiabetic agents).

2.4. Statistical analysis

Data were expressed as mean ± standard deviation. Differences of the means were evaluated using one-way analysis of variance (ANOVA) for continuous variables and chi-square test for categorical variables. Bonferroni's post hoc test was performed for multiple comparisons when significance was observed across groups in ANOVA. Multiple linear regression analysis was performed to evaluate the association between adiponectin, ghrelin, leptin and each metabolic component according to SCTs. Age (continuous), sex, BMI (continuous), smoking status (never, former, and current smoker), physical activity (MET-hour/day; continuous), and alcohol consumption (g/day; continuous) were included as covariates in multiple models. Furthermore, a multiple logistic regression analysis was conducted to evaluate the odds ratio (OR) for MetS in relation to two adipokines and ghrelin according to SCTs with a 95% confidence interval (CI) and *P* value. Covariates in the multiple logistic regression analysis were the same as those in multiple regression models. All statistical analysis was performed using SAS version 9.3 (SAS Institute, Cary, North Carolina, USA). *P*-values less than 0.05 were considered statistically significant.