Maturitas 74 (2013) 148–153

Contents lists available at SciVerse ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Total testosterone and sex hormone-binding globulin are associated with metabolic syndrome independent of age and body mass index in Korean men

Doohee Hong[a], Young-Sang Kim[b], Eun Soo Son[a], Kyu-Nam Kim[a], Bom-Taeck Kim[a], Duck-Joo Lee[a], Kwang-Min Kim[a,*]

[a] Department of Family Medicine, Ajou University School of Medicine, 164 Worldcup-ro, Yeongtong-gu, Suwon, Gyeonggi-do 443-721, Republic of Korea
[b] Department of Family Medicine, Cha University School of Medicine, 59 Yatap-ro, Bundang-gu, Seongnam, Gyeonggi-do 463-712, Republic of Korea

ARTICLE INFO

Article history:
Received 9 May 2012
Received in revised form 8 October 2012
Accepted 20 October 2012

Keywords:
Testosterone
Sex hormone-binding globulin
Metabolic syndrome
Korean

ABSTRACT

Objective: The purpose of this study is to investigate the relationship between sex hormones and metabolic syndrome independent of age and BMI in Korean men.
Study design: We conducted a cross-sectional study with data from a health promotion center during the period from March 2007 to February 2010. 2172 Korean men aged 21–79 were enrolled. Total testosterone, sex hormone-binding globulin (SHBG), high density lipoprotein (HDL) cholesterol, triglyceride (TG), and glucose were assessed with overnight fasting serum samples.
Main outcome measures: Sex hormones were divided into quartiles; odds ratios for metabolic syndrome and each component were analyzed.
Results: Total testosterone showed negative associations with waist circumference (WC), fasting glucose, TG, blood pressure and body mass index (BMI), and a positive relationship with HDL cholesterol (*P* for trend <0.001, respectively). SHBG was negatively associated with WC, fasting glucose, TG, and BMI, and positively associated with total testosterone and age. Comparing with the highest quartile, odds ratios of lowest quartile of total testosterone and SHBG for metabolic syndrome were 3.01 (95% CI, 2.11–4.28) and 6.34 (95% CI, 2.29–17.58), respectively, after adjusting for age, smoking status, alcohol intake, exercise, and BMI. Total testosterone was significantly associated with each metabolic component and SHBG was associated with glucose and TG after adjustment for age, smoking status, alcohol intake, and BMI. Calculated free testosterone had no significant relationship with metabolic syndrome or its components.
Conclusion: Total testosterone and SHBG are negatively associated with prevalence of metabolic syndrome independent of age and BMI in Korean men.

1. Introduction

The prevalence of metabolic syndrome has been increasing in many countries. In the U.S., the prevalence of metabolic syndrome increased from 29.2 to 34.2% according to data comparing the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) with NHANES 1999–2006 [1]. Data from Asian-Pacific countries showed increasing prevalence of metabolic syndrome [2]. In accordance with data from other countries, the prevalence of metabolic syndrome in Korea has been increasing from 24.9% in 1998 to 31.3% in 2007 [3].

The close relationship of low total testosterone and sex hormone-binding globulin (SHBG) levels with metabolic syndrome has been founded in both cross-sectional studies [4,5] and longitudinal studies [6,7]. Low total testosterone was associated with an increased risk of developing metabolic syndrome over time, in non-overweight, middle-aged men [8]. These studies led to clinical implications that low sex hormone levels might be a risk factor for metabolic syndrome.

It is well-known that low levels of total testosterone and SHBG increase insulin resistance [9]. Inversely, high testosterone level is independently associated with an increased insulin sensitivity and a reduced risk of metabolic syndrome [4]. Recent studies have showed that low testosterone and SHBG were strongly associated with an increased likelihood of metabolic syndrome, independent of traditional cardiovascular risk factors and insulin resistance [10,11].

Total testosterone refers to the sum of SHBG-bound testosterone with low affinity, albumin-bound testosterone with high affinity, and free testosterone. However, it is not clear which component of testosterone has a primary role for development of metabolic syndrome. The association of free testosterone and metabolic syndrome has been inconsistent, whereas SHBG has demonstrated a constant inverse relationship with metabolic syndrome [4,6,7,10].

* Corresponding author. Tel.: +82 31 219 5306; fax: +82 31 219 5218.
E-mail address: gaksi@ajou.ac.kr (K.-M. Kim).

0378-5122/$ – see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.maturitas.2012.10.016

Many studies on sex hormones and metabolic syndrome have been performed throughout the world, but relatively a few studies have been conducted involving Asian subjects [11–13]. Definition of metabolic syndrome for Asians differs from that of Caucasians as cutoff points for central obesity is different [14]. The aim of this large-scale cross-sectional study is to assess the significance of sex hormones in relation to metabolic syndrome among healthy Korean men.

2. Methods

2.1. Subjects

This study was a cross-sectional, single center study of 2874 men. We reviewed data of subjects who visited Ajou University Hospital during the period from March 2007 to February 2010 for their routine medical examination. Among these, men who were already receiving testosterone replacement therapy, or corticosteroid, had medical histories of malignancies or asthma, had abnormal results of liver or thyroid function tests, and diagnosed with liver cirrhosis were excluded. Participants with high testosterone above 35 nmol/L (age ≥50) and 45 nmol/L (age <50) were excluded. Since routine examination was undertaken annually or biannually, overlapped data were also excluded. The final analysis for the study was performed in 2172 men. The present study was approved by Institutional Review Board of Ajou University Hospital (AJIRB-MED-MDB-11-386) and written informed consent was obtained from each individual.

2.2. Anthropometry and data collection

Current and past medical conditions were obtained from self-report questionnaires. Height and weight (0.1 kg units) measurements were taken with light clothes on. BMI was calculated with measured height and weight (kg/m^2). Waist circumference was measured at the central part between the 12th rib and iliac crest by trained personnel. Blood pressure was measured after 10 min of rest in a sitting position using an automatic sphygmomanometer (TM-2655P, P.M.S. (Instruments) Ltd., Berkshire, U.K.). Overnight fasting blood samples were drawn from the antecubital area. Glucose, triglyceride (TG), high density lipoprotein (HDL) cholesterol were measured using an automatic analyzer (Toshiba TBA 200FR, Toshiba Medical Systems Co. Ltd., Tokyo, Japan). Total testosterone was measured by radioimmunoassay using Coat-a-Count Total Testosterone (Siemens Healthcare Diagnostic Inc., NY, USA). SHBG was determined by radioimmunoassay using SHBG IRMA kit (Beckman Coulter Inc., CA, USA). Free testosterone was calculated from serum total testosterone, SHBG and albumin concentrations using the method proposed by Vermeulen et al. [15]. Current smoker was defined as an individual who regularly smoked at least one cigarette a day. Alcohol user included a social drinker except a person who never drank in the past 3 months. Exercise meant exercise was done at least once a week on a regular basis.

2.3. Metabolic syndrome

The definition of metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III (ATP NCEP III) criteria for Asians was defined as the presence of three of more of the following: (1) waist circumference more than 90 cm; (2) systolic blood pressure at least 130 mmHg or diastolic blood pressure at least 85 mmHg or antihypertensive medication use; (3) high-density lipoprotein cholesterol less than 40 mg/dl or lipid medication use; (4) triglyceride more than 150 mg/dl; and (5) elevated fasting blood glucose more than 110 mg/dl or taking hypoglycemic agents.

Table 1
General characteristics of the study subjects.

	Adult men aged 21–79
n	2172
Age (years)	49.4 ± 8.8
Waist circumference (cm)	85.6 ± 7.6
Fasting glucose (mmol/L)	5.07 ± 1.32
Triglyceride (mmol/L)	1.52 ± 1.05
HDL cholesterol (mmol/L)	1.29 ± 0.30
Systolic blood pressure (mmHg)	121.5 ± 13.9
Diastolic blood pressure (mmHg)	81.6 ± 10.3
Body mass index (kg/m^2)	24.5 ± 2.9
Total testosterone (nmol/L)	16.92 ± 5.30
SHBG (nmol/L)[a]	52.8 ± 19.3
Free testosterone (pmol/L)[a]	262.6 ± 80.3
Number of metabolic syndrome components	1.5 ± 1.2
Metabolic syndrome prevalence (%)	20.4
AST (U/L)	25.4 ± 9.1
ALT (U/L)	29.9 ± 15.7
Current smoker (%)	43.7
Alcohol use (%)	77.2
Exercise (%)	48.6

Data are mean ± standard deviation unless otherwise indicated. HDL: high density lipoprotein; SHBG: sex hormone-binding globulin; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

[a] *n* = 273.

2.4. Statistical analysis

The values were expressed as mean ± standard deviation or % for descriptive statistics. Mean differences of total testosterone between metabolic syndrome group and reference group were assessed with independent *t*-test. Testosterone, sex hormone-binding globulin, and calculated free testosterone were divided into quartiles; the divided groups were compared by ANOVA test. Different metabolic syndrome prevalence according to quartiles was calculated by chi-square test considering linear by linear association. The relationship between total testosterone, SHBG, calculated free testosterone quartiles and metabolic syndrome were assessed with logistic regression analysis after adjusting for age, BMI, smoking status, alcohol intake, and exercise. OR and 95% CI were assessed for metabolic syndrome and each metabolic syndrome component. Statistical data were analyzed using SPSS for Windows version 18 (SPSS Inc., Chicago, IL, USA). A P-value <0.05 was considered significant.

3. Results

The mean age of the subjects was 49.4 ± 8.8 yr and the prevalence of metabolic syndrome was 20.4%. The mean total testosterone, SHBG, calculated free testosterone were 16.92 ± 5.30 nmol/L, 52.8 ± 19.3 nmol/L, 262.6 ± 80.3 pmol/L, respectively (Table 1). The mean total testosterone of metabolic syndrome group was lower than that of non-metabolic syndrome group (15.22 ± 4.42 nmol/L vs. 17.36 ± 5.42 nmol/L, $P < 0.001$, data not shown).

3.1. Parameters of metabolic syndrome according to sex hormone quartiles

Total testosterone, SHBG, and calculated free testosterone were divided into quartiles. Mean values of metabolic syndrome components for each quartile are presented in Table 2. Mean values of waist circumference, fasting glucose, TG, systolic/diastolic blood pressure, BMI, and the number of metabolic syndrome components decreased while HDL cholesterol increased significantly as total