Clinica Chimica Acta 487 (2018) 275–280

Contents lists available at ScienceDirect

Clinica Chimica Acta

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

Contribution of obesity as an effect regulator to an association between serum leptin and incident metabolic syndrome☆

Jung Ran Choi[a], Jang Young Kim[a,b], Ji Hye Huh[b], Sang Ha Kim[b], Sang Baek Koh[a,c,*]

[a] Institute of Genomic Cohort, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea
[b] Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea
[c] Department of Preventive Medicine, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea

ARTICLE INFO

Keywords:
Leptin
Body mass index
Obesity
Effect regulator
Metabolic syndrome

ABSTRACT

Background: We investigated whether serum leptin can be a predictor for incident cases of MetS in a population-based study.
Methods: This is a prospective cohort study of 1590 adults aged between 40 and 70 years, who did not have MetS in 2005–2008 (at baseline) and 2008–2011 (follow-up). The baseline serum leptin concentrations were measured by radioimmunoassay.
Results: During an average of 2.8 years of follow-up, 113 men (17.1%) and 148 women (15.9%) developed MetS. In multivariable adjusted models, the odds ratio of incident MetS when comparing the lowest to the highest quartiles of leptin levels was 3.17 in men and 2.79 in women; nevertheless, the significance disappeared after adjusting for the body mass index (BMI). In subsidiary analyses by BMI, logistic regression analysis showed that subjects with the highest tertile of serum leptin level were 3.04 and 2.12 times more likely to have MetS than those with the lowest tertile in lean subjects (OR 3.04; 95% CI 1.44–6.41; $p = .004$ in men vs. OR 2.12; 95% CI 1.06–4.25; $p = .036$ in women, respectively).
Conclusions: Obesity is an effect regulator, which can predict an association between increased serum leptin level and the incidence of MetS in lean subjects.

1. Introduction

The metabolic syndrome (MetS) comprises a cluster of cardiometabolic risk factors, with insulin resistance and increased adiposity as its central features [1–3]. Identifying individuals with MetS is important due to its association with the increased risk of atherosclerotic cardiovascular disease and type 2 diabetes mellitus (T2DM) [4–6]. Given the high prevalence of MetS and its potential consequences, there is substantial interest in understanding its causes and mechanisms in population-based longitudinal studies.

Since MetS is closely linked to obesity and adipose tissue dysfunction, attention was focused on the visceral adipose tissue production of cytokines (adipokines), which are strong candidates that may predict the development of MetS in the future. Leptin is one of these adipokines that is secreted mainly by the white adipose tissue [7]. Circulating leptin is a key regulator that serves to communicate the state of body energy repletion to the central nervous system in order to suppress food intake and permit energy expenditure [7,8]. Adequate leptin concentrations permit energy expenditure on the processes of reproduction, tissue remodeling, and growth and similarly regulate the autonomic nervous system, other elements of the endocrine system, and the immune system.

Serum leptin concentrations are higher in people with obesity than in normal weight subjects due to the decreased sensitivity to leptin. Serum leptin concentrations highly correlate with the percentage of body fat, and serum leptin concentrations are reduced by weight loss and negative caloric balance [9,10]. These findings suggest that leptin concentrations may play a role in the development of metabolic abnormalities.

Recently, obesity has been identified as a modifier between the association of leptin concentrations and cardiovascular (CV) events [11]. Lower leptin concentrations predicted CV events in lean patients. In contrast, in patients with obesity, higher leptin concentration was a predictor of CV events [11], or there were no association between leptin

☆ Author contributions: Jung Ran Choi and Jang Young Kim contributed to this manuscript equally.

* Corresponding author at: Department of Preventive Medicine, Yonsei University Wonju College of Medicine, 20 Ilsan-ro, Wonju, Gangwon-do 220-701, Republic of Korea.
E-mail address: kohhj@yonsei.ac.kr (S.B. Koh).

https://doi.org/10.1016/j.cca.2018.09.038
Received 19 June 2018; Received in revised form 19 September 2018; Accepted 29 September 2018
Available online 02 October 2018
0009-8981/

and CV events [11]. However, prospective studies of the predictive value of serum leptin to identify individuals at high risk of new-onset MetS are lacking.

2. Methods

2.1. Study population

We used data from 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 to assess the prevalence, incidence and risk factors for chronic degenerative disorders such as hypertension, diabetes, osteoporosis, and CV disease [12–14]. To the KoGES-ARIRANG study, all adults residing in rural areas of Wonju and Pyengchang in South Korea, where demographic shifts are infrequent and the population can be followed long-term, were invited to participate in the study.

The baseline survey, carried out from November 2005 to January 2008, included 5178 adults (2127 men and 3051 women) aged 40–70 ys. All study participants were invited to the first follow-up survey (April 2008 to January 2011), of whom 3862 (74.6%) attended. We then excluded 1545 participants with MetS at baseline, 695 participants without baseline leptin measurements, 20 participants with any history or presence of CV disease at baseline, and 12 participants with incomplete data. The final sample size for the present analysis was 1590 participants (661 men and 929 women) without MetS at baseline (Fig. 1). The study protocol was approved by the Institutional Review Board of Wonju Christian Hospital. All participants provided written informed consent.

2.2. Data collection

At baseline and at the follow-up examination, study participants completed a standardized medical history and lifestyle questionnaire and underwent a comprehensive health examination according to standard procedures. Body weight and height were measured, while participants were wearing light indoor clothing without shoes. Waist circumference was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest using a tape measure (SECA-200, SECA). Systolic (SBP) and diastolic blood pressures (DBP) were measured twice in the right arm using a standard mercury sphygmomanometer (Baumanometer). The mean of the 2 blood pressure readings was used for data analyses. Smoking status was determined based on self-report. Never-smokers were defined as participants who had smoked < 100 cigarettes (< 5 packs of cigarettes) in their lifetime. Current smokers were defined as participants who had smoked ≥100 cigarettes in their lifetime and who reported “currently smoking” in the questionnaire. Former smokers were defined as participants who had smoked ≥100 cigarettes in their lifetime but who reported “abstain from smoking” in the questionnaire.

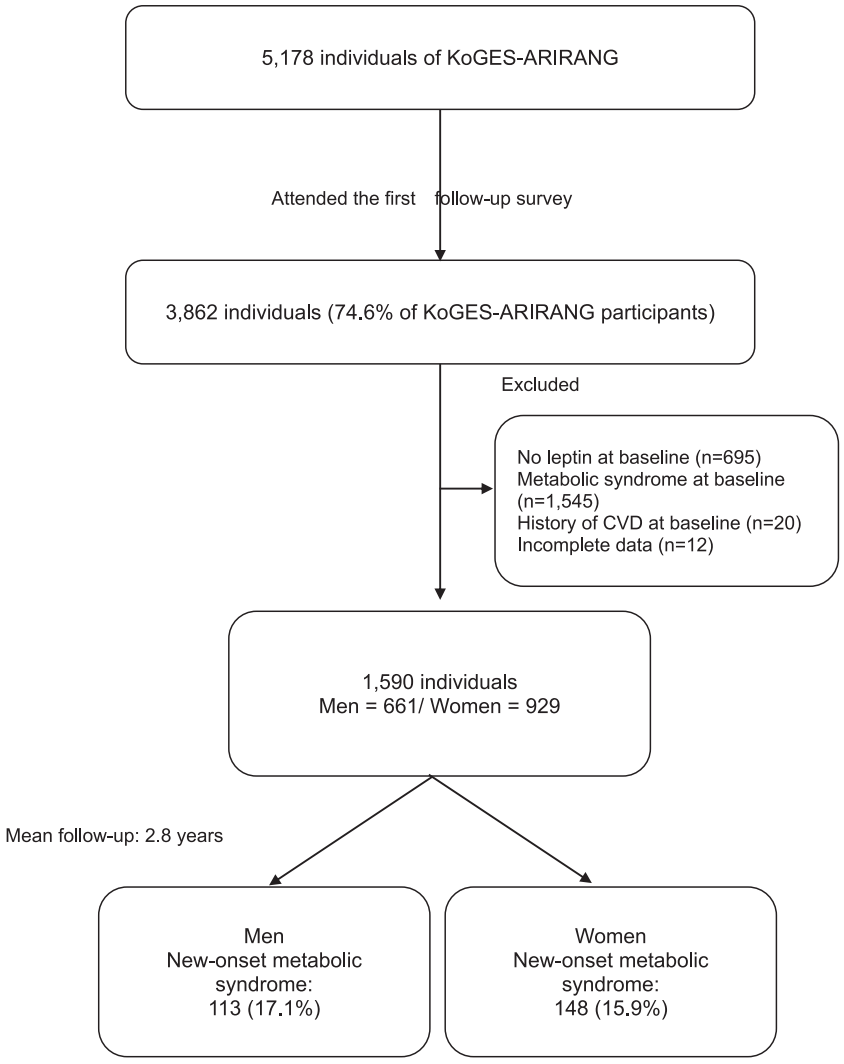

Fig. 1. Flow chart of the participants in the KoGES-ARIRANG study.