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Original Article

Leptin as an important link between obesity and cardiovascular risk factors in men with acute myocardial infarction

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ABSTRACT

Objective: The levels of leptin, a major regulator of lipid metabolism, may increase in obesity, and contribute to the development of metabolic syndrome. Leptin is produced by adipose tissue and is a peptide hormone, which has strong association with obesity, elevated cardiovascular risk, and morbidity. The present study was designed to evaluate the relationships between leptin levels, obesity, and cardiovascular risk factors in men with acute myocardial infarction.

Methods and results: Twenty-four obese and twenty-three nonobese male patients, who had experienced their first myocardial infarction, were included in the study. Their leptin levels, biochemical parameters, and anthropometric measures were obtained. Mean leptin levels were significantly higher in the obese group compared to the nonobese group (2.53 ng/mL versus 1.23 ng/mL; $p < 0.01$). Leptin levels correlated positively with anthropometric measurements, triglyceride, fasting glucose, C-reactive protein, and uric acid levels, and negatively with high-density lipoprotein cholesterol levels.

Conclusion: Findings indicate high leptin levels to be positively correlated with obesity and diastolic blood pressure in male patients with myocardial infarction.

1. Introduction

Obesity is associated with a high risk of developing cardiovascular (CV) and metabolic diseases, such as hypertension, coronary atherosclerosis, myocardial hypertrophy, diabetes, dyslipidemia, and increased CV morbidity and mortality.[1] Leptin is a 16-kDa polypeptide (167 amino acids) hormone synthesized and secreted into the circulation primarily by white adipocytes.[2,3] There is a strong relationship between body fat mass and the amount of synthesized and secreted leptin.[4,5] Leptin is considered to be an antiobesity hormone. The first

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major action of leptin to be described is the control of body weight and fat deposition through its effects on hypothalamic receptors, which leads to appetite inhibition, as well as its effects on metabolic rate stimulation and thermogenesis.[2,3] Leptin levels decrease during fasting and increase after several days of overfeeding, in a mechanism that helps to regulate energy balance in humans. Thus, increased leptin concentrations would be expected to correlate with decreased weight. However, serum leptin levels are in fact strongly correlated with body fat mass in obese individuals. Recent studies suggest the existence of an endogenous leptin-resistance mechanism in obesity[6] that may explain this unexpected correlation.

In obesity, elevated leptin levels are not sufficient to prevent disturbances in energy balance, suggesting that obese people are leptin-resistant.[7] Alternatively, another possibility is that nonleptin-mediated mechanisms play a more powerful role than leptin under the altered physiological conditions present in obesity. Obesity is associated with increased sympathetic nerve activity, and leptin, partly by increasing renal sympathetic nerve activity, has been proven to participate in autonomic nervous system control. Therefore, the contribution of leptin to sympathetic activation in a leptin-resistant state, like obesity, is contradictory. This has led to the novel concept of selective leptin resistance, in which resistance appears to be primarily limited to the metabolic (satiety and weight-reducing) functions of leptin, sparing the other functions in obese individuals.[8]

It has been suggested that leptin could be an important link between obesity and the development of CV diseases.[9] This might be mediated through various effects of leptin, including effects on blood pressure,[10] platelet aggregation,[11] formation of arterial thrombosis,[12] and inflammatory vascular response.[13] High levels of leptin are believed to be associated with reduced arterial distensibility, an index of circulatory function, and leptin is involved in the pathogenesis of the atherosclerotic process through mechanisms other than vascular relaxation.[14] Leptin has also been shown to promote angiogenesis, regulate osteoblastic differentiation, enhance the calcification of vascular cells, and potentiate prothrombotic platelet aggregation through a novel leptin receptor mechanism.[11]

Several studies have shown leptin to be a predictor of myocardial infarction, coronary events, and stroke, independent of body mass index (BMI).[15,16] Plasma leptin was observed to be higher in individuals with a paternal history of premature myocardial infarction than in those without family history of CV events.[17] Plasma leptin was also higher in male patients, who subsequently developed first-ever myocardial infarction than in control subjects.[16]

The aim of the present study was to assess the relationships between blood leptin concentrations and several anthropometric parameters and CV risk factors in obese and nonobese men with acute myocardial infarction (AMI) treated with primary coronary intervention (PCI).

2. Methods

2.1. Study population

The study subjects included 24 obese male patients and 23 age-matched nonobese men as the control group, who experienced their first acute myocardial infarction. Patients who had previous ischemic heart disease, atrial fibrillation, bundle branch block, and significant valvular heart disease, or who were >65 years of age, were excluded from the study.

Ethical approval was taken from local ethics committee.

Anthropometric measurements, clinical definitions, and treatment.

AMI was diagnosed on the basis of symptoms, electrocardiographic signs, and elevation of myocardial injury markers.

A BMI of 30, calculated as body weight divided by the square of height (kg/m^2), was used as the cutoff value for obesity. Patients with a BMI <25 were designated as nonobese. Weight and height were measured on the third or fourth day after admission, while the subjects were fasting and wearing only their undergarments. Waist circumference (WC), a measure of abdominal subcutaneous and visceral fat, was measured at the widest diameter between the xiphoid process of the sternum and the iliac crest. Hip circumference (HC), representing subcutaneous fat alone, was measured at the widest diameter over the greater trochanters. From these measurements, the waist-to-hip ratio (WHR) was calculated. Systolic and diastolic blood pressures (SBP, DBP) were measured before blood sampling.

2.2. Laboratory measurements

C-reactive protein (CRP) and uric acid levels were assessed as part of a complex analysis of the blood samples taken upon admission to the hospital. Fasting blood glucose levels, lipid profile and leptin levels were determined from the blood drawn the following day. Plasma samples taken for leptin concentration measurement were frozen at −70 °C, until analysis with a sandwiched enzyme-linked immunosorbent assay (ELISA) (ELx 800 Absorbance Microplate Reader [BioTek, Winooski, USA] and Assay Max Human Leptin ELISA Kit [Assaypro, St. Charles, MO, USA]).

2.3. Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) for Windows (version 15.0; SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean ± standard deviation. Variables were log-transformed before statistical analysis, if necessary. Comparison between the two groups was performed using the two-tailed, nonpaired student's *t*-test or the Mann–Whitney test, as appropriate. Categorical variables were presented as numbers or percentages, and were analyzed using the chi-square test. Association between the parameters was assessed using the Spearman correlation coefficient. A p value <0.05 was considered statistically significant.

3. Results

The proportion of patients with hypertension and smoking were similar in the two groups, as were SBP levels. The proportion of patients with high-density-lipoprotein cholesterol (HDL-CH) <40 mg/dl, total CH >200 mg/dl, and triglycerides (TG) >150 mg/dl were significantly higher in the obese group than in the control group, as were the anthropometric