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Original article

Role of serum leptin in the severity of coronary artery disease in patients with stable angina☆

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ABSTRACT

Background and objectives: Leptin is a plasmatic peptide hormone that has been related to cardiovascular homeostasis and atherosclerosis but much is still unknown about its relationship with coronary artery disease. The aim of this study was to evaluate the value of serum leptin in patients with stable angina and its relationship with the severity of coronary disease.
Patients and methods: 204 patients, 152 with stable angina (coronary artery disease group) and 52 without coronary disease excluded by cardiac computerized tomography (control group) were included. The coronary artery disease group was divided into 2 subgroups according to severity of coronary disease (single or multivessel disease, 46 and 106 patients, respectively). Serum leptin levels were determined by Enzyme-Linked InmunoSorbent Assay.
Results: Leptin levels were significantly higher in patients with multivessel disease and were independently associated with a greater severity of coronary artery disease when compared with controls (OR 1.14; 95%CI: 1.03–1.27; $p = 0.014$) and with patients with single vessel disease (OR 1.12; 95%CI: 1.01–1.25; $p = 0.036$). Serum leptin was tested as a diagnostic marker of multivessel disease with an area under the curve obtained from Receiver Operating Characteristics of 0.6764 (95%CI 0.5765–0.7657).
Conclusions: Serum leptin levels were associated in patients with stable angina with the severity of coronary artery disease, suggesting its value in the development of coronary disease and as a future therapeutic target.

Papel de la leptina sérica en la gravedad de la enfermedad coronaria en pacientes con angina estable

Palabras clave:
Enfermedad arterial coronaria
Leptina
Angina estable

RESUMEN

Fundamentos y objetivo: La leptina es una hormona plasmática que ha sido relacionada con la homeostasis cardiovascular y la aterosclerosis, pero no existen datos concluyentes sobre su asociación con la patogénesis de la enfermedad coronaria. El objetivo de este estudio fue evaluar el valor de la leptina sérica en pacientes con angina estable y su relación con la gravedad de la enfermedad coronaria.

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Pacientes y método: Se incluyeron 204 pacientes, 152 con angina estable (grupo con enfermedad coronaria) y 52 sin enfermedad coronaria, excluida por tomografía computarizada cardíaca (grupo control). El grupo con enfermedad coronaria fue dividido en 2 subgrupos atendiendo a la gravedad de la afectación (enfermedad monovaso o multivaso, 46 y 106 pacientes respectivamente). Los niveles de leptina sérica fueron determinados mediante *Enzyme-Linked Inmunosorbent Assay*.
Resultados: Los niveles de leptina fueron significativamente superiores en los pacientes con enfermedad multivaso y se asociaron de forma independiente con una mayor gravedad de la enfermedad coronaria en comparación con los controles (OR 1,14; IC95% 1,03-1,27; p = 0,014) y con pacientes con enfermedad monovaso (OR 1,12; IC95% 1,01-1,25; p = 0,036). Se testó el valor diagnóstico de la leptina sérica para el diagnóstico enfermedad multivaso, obteniendo un área bajo la curva en la curva *Receiver Operating Characteristic* de 0,6764 (IC95% 0,5765-0,7657).
Conclusiones: La leptina sérica se asoció en pacientes con angina estable con la mayor gravedad de la enfermedad coronaria, mostrando su implicación en el desarrollo de la enfermedad coronaria y como futuro objetivo terapéutico.

Introduction

Coronary artery disease (CAD) continues to be the leading cause of death in the Western world. Multiple cardiovascular risk factors are involved in its pathophysiology, and their adequate management is fundamental to treatment and both primary and secondary prevention.[1] However, despite a strict and optimal control of these factors, many CAD patients with stable angina are forced to undergo invasive coronary procedures because of the progression of their disease, which results in significant health costs and affects their quality of life.[2]

Leptin is a peptide hormone derived from adipose tissue, which was first described in a study conducted on rodents exploring the pathophysiology of obesity.[3] Leptin acts by regulating the deposit of fatty tissue in the body, being able to decrease appetite and increase energy expenditure,[4,5] through a specific receptor in the hypothalamus.[6] For this reason, leptin deficiency causes obesity in mice and rats.[4,5] However, this condition is very rare in humans.[7] Generally, obese patients have increased concentrations of plasma leptin, suggesting a peripheral resistance to action.[8]

In addition, leptin has been implicated in the regulation of different peripheral actions, including control of cardiovascular homeostasis.[9] Several studies have shown a positive correlation between high levels of circulating leptin and risk of cardiovascular disease,[10–12] and proatherosclerotic has been identified as a factor.[13] However, the net effect of leptin on cardiovascular pathophysiology, particularly in CAD, is controversial and has not yet been fully explained. The purpose of this study was to determine the value of leptin in a specific population of patients with stable angina and its relationship to CAD severity.

Patients and methods

Patient selection

The CAD group (CADG) was selected from a population of patients with stable angina undergoing percutaneous coronary intervention. In order to avoid limitations of age, patients older than 75 years were also included. The control group (CG) was a population of patients without CAD, demonstrated by cardiac computed tomography (CT), adjusted for age, gender and cardiovascular risk factors. This study was approved by the Malaga Research Ethics Committee in accordance with the Helsinki Declaration. All patients gave written informed consent.

Determination of leptin

Blood samples were collected for each patient during coronarography for the CADG and after CT for the CG. Leptin concentration (ng/ml) was determined by Enzyme-Linked Inmunosorbent Assay.

Coronary angiography

The diagnostic coronary angiography was performed by expert cardiologists at the Hemodynamic Laboratory at the Hospital Universitario Virgen de La Victoria in Malaga. Multi-vessel disease (MVD) was defined as the main 50% coronary stenosis of the lumen vessel in two or more of the three major epicardial branches or one of its branches more than 2 mm in diameter. Stenosis of these coronary is considered single vessel disease.

Cardiac computed tomography

The cardiac CT was performed using a device with 64 slices and the obtained images were assessed by two experienced specialists (a radiologist and a cardiologist). The CT images were analyzed considering the calcium score of the coronary arteries and the degree of stenosis. Patients who did not have significant stenotic lesions were selected for the CG. Significant stenosis was understood to be when there was a narrowing of the lumen vessel greater than 50%.

Statistical analysis

The normality of the variables was established by the Kolmogorov–Smirnov test. Quantitative variables were presented as mean ± standard deviation or mean (interquartile range) attending to normal distribution, and qualitative variables were expressed as absolute value (percentage). Quantitative variables were compared using the Student *t* test or ANOVA and qualitative variables with the chi-square test. The linear trend was tested using ANOVA polynomial test or Jonckheere-Terpstra test. The analysis of correlations was established using the Spearman's rho test. A study of multivariate logistic regression in which the odds ratio (OR) and confidence intervals were calculated at 95% (95% CI) to establish the relationship between leptin levels and severity of coronary disease was carried out for the entire sample, separated by gender. The diagnostic yield was expressed according to sensitivity, specificity, positive predictive value and negative predictive value. Receiver Operating Characteristic (ROC) curves were constructed and the Area Under the Curve (AUC) was calculated to analyze the diagnostic accuracy of the leptin levels according to the severity of coronary impairment for the entire sample, separated by gender. The curves were compared using the Hanley and McNei test. The study was performed using the statistical program SPSS, version