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Serum Leptin In Ischemic Heart Disease Patients with and without Significant Diastolic Dysfunction In Lean and Obese Patients; Cross Sectional Study

Thesis

Submitted for partial fulfillment of the Master Degree in Cardiology

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Abstract

Background Cardiovascular diseases represent the leading cause of mortality worldwide. Ischemic heart disease is one of the main causes of diastolic heart failure and its presence predicts a poor prognosis in ischemic heart patients. Most cardiovascular diseases can be prevented by addressing behavioral risk factors such as overweight and obesity. Leptin –also known as satiety hormone- helps in inhibiting hunger and regulate energy balance

Objective to correlate leptin level with ischemic heart disease with or without diastolic dysfunction by comparing it in lean and obese patients.

Material and Methods from June 2019 to November 2019, 140 ischemic patients documented with CA, MSCT or history of PCI AND 35 Control subjects were enrolled from both Ain Shams University, Cardiology department wards and outpatient clinic and Misr University for science and technology, cardiology department wards and outpatient clinic. All participants subjected to history, clinical examination, Duke CAD index to estimate the severity of ischemia, calculation of their BMI, blood sampling for measuring their serum leptin level and echocardiography for detecting the diastolic function. Patients were divided into four groups according to their BMI and Diastolic function in addition to the control group. Groups were demonstrated as follow Group A lean ischemic patients without significant diastolic dysfunction, Group B lean ischemic patients with diastolic dysfunction (II-IV), Group C obese ischemic patients without significant diastolic dysfunction, Group D obese ischemic patients with diastolic dysfunction(II-IV), Group E is a control group lean non ischemic without diastolic dysfunction.

Results: There were significant positive correlations between serum leptin and Duke score in all ischemic groups (n=140) (p<0.001). Serum leptin abnormality was significantly more frequent in diastolic dysfunction groups (n=70) than in non-dysfunction groups (N=70) (Group B 25.7%, group D 28.6% vs group A 5.7% group C 8.6%, also was lowest in control group (n=35) 0.0%. serum leptin was significantly positive correlated with ischemia as in group A17.8±2.1ng/mL group B 23.4±11.1ng/mL group C 55.4±10.9 ng/mL group D 65.2±10.8 ng/mL vs control group E 13.1±2.7 ng/mL.

Conclusion: leptin is an independent risk factor for coronary heart disease. Also elevated plasma leptin levels are associated with impaired left ventricular diastolic function in patients with CAD independently of obesity and other confounding variables.

Key words: serum leptin, diastolic dysfunction, coronary heart disease.

Abbreviation list: CA coronary angiography, MSCT multi-slice computed tomography, PCI percutaneous cardiac intervention, BMI body mass index, CAD coronary artery disease.

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List of Abbreviations

 α -MSH : α -melanocyte-stimulating hormone

apoEBBBBlood brain barrierBMIBody mass index

CA : Coronary angiography
CAD : Coronary artery disease
CBC : Complete blood count

CCK : Cholecystokinin

CHD : Coronary heart disease

cm : Centimeter

CSF : Cerebrospinal fluid

CT : Computed Tomography
CVD : Cardiovascular disease
DD : Diastolic dysfunction
DNA : Deoxyribonucleic acid

DT : Deceleration time
DXA : Dual-energy X-ray
ECG : Electrocardiography

EDPVR : End-diastolic pressure-volume relationship

GLP-1 : Glucagon-like peptide 1

HbA1c : Hemoglobin A1c

HDL : High density lipoprotein

HF : Heart failure

HFpEF : Heart failure with a preserved ejection fraction

HTN : Hypertension

ID : Ischemic with diastolic dysfunction

IHD : Ischemic heart disease

IND : Ischemic without diastolic dysfunction

IVRT : Isovolumic Relaxation Time

JAK-STAT3: Janus Kinase-Signal Transducer and

Activator of Transcription-3

JNK : Jun Nuclear Kinase

Kcal : Kilocalorie

KFT : Kidney function test

Kg : kilogram

Kg/m² : Kilogram/ meter squared

LAP : Left atrial pressure

LDL : Low density lipoprotein

LV : Left ventricle

LVDD : Left ventricular diastolic dysfunction

LVDD-PEF : Left ventricular diastolic dysfunction with

preserved ejection fraction

LVEDVI LV : Left ventricular end-diastolic volume index

LVEF : Left ventricular ejection fraction MAPK : Mitogen-activated protein kinase

MetS : Metabolic syndromeMI : Myocardial infarctionmmHg : Millimeters of Mercury

MSCT : Multislice computed tomography

ng / ML : Nanograms per milliliter

NIND : Non ischemic without diastolic dysfunction

PCI : Percutaneous coronary intervention

PW: Pulsed wave PYY: Peptide YY

SLR : Soluble leptin receptors

TD : Tissue Doppler

TDI : Tissue Doppler index

TNF-α : Tumor necrosis factor alphaVLDL : Very low density lipoproteinWHO : World health organization

WHR : Waist hip ratio

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Introduction

Leptin -also known as satiety hormone- helps in inhibiting hunger and regulate energy balance, that's why the body does not trigger hunger responses when it does not need energy (1). It is one of the most important adipocytokine modulating metabolism by regulating energy balance and appetite ⁽²⁾. Most authors proved that the Leptin is an important hormone against obesity. Suggesting that the use of leptin therapy may be possible to prevent obesity and diseases like hypertension and diabetes mellitus even before their occurrence (3). Apart from metabolism, leptin exhibits systemic effects that includes lipolysis, immune modulation, helps blood pressure regulation as well it helps in wound healing and angiogenesis ⁽⁴⁾. Leptin activates sympathetic nervous system, participates in thrombosis and platelets aggregation as well and that's how it was linked to ischemic heart disease (5).

Meta-analysis performed in 2014 showed that serum leptin level was more statistically different in males than females in Ischemic heart diseases ⁽⁶⁾. Yet, Puurunen concluded that hyperleptinemia is associated with left ventricular diastolic dysfunction in patients with ischemic heart disease and may be sole mechanistic link connecting

the development of congestive heart failure in obese subjects ⁽⁷⁾. The immune modulation of leptin stimulating inflammatory response by activating TNF-α via p38 and JNK MAPK pathway and these inflammatory markers may be associated with the risk of recurrent myocardial infarction and death ⁽⁷⁾.