Impact of Visceral Obesity and Plasma Apelin Level on Coronary Artery Disease in Egyptian Patients

Thesis

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ABSTRACT

Background: Distribution of body fat is known to be more independent and potent predictor of morbidity and mortality than total body adiposity, individuals with abdominal obesity are at a great risk for developing type 2 diabetes mellitus and atherosclerotic cardiovascular disease. Apelin could be considered a 'good' adipokine when considering cardiovascular disease. It reduces atherogenesis, macrophage inflammation, mean arterial pressure, cardiomyocyte contractility, atrial fibrillation and heart failure.

Objectives: To assess the impact of visceral obesity and plasma level of apelin on coronary artery disease in Egyptian patients.

Patients and methods: A total of 371 patients were recruited in this observational study, mean age was (53.6± 9), males were 229(61.7%) and 142(38.3%) were females scheduled for elective coronary angiography in Kaser alainy teaching hospital and national heart institute for the period between December 2012 and May 2013. All patients were subjected to thorough history taking including sex, history of smoking, diabetes, hypertension and family history of coronary artery disease, reason for coronary angiography and any previous history of peripheral vascular disease, myocardial infarction , congestive heart failure, chronic obstructive pulmonary disease, analysis of lipid profile, measurement of serum creatinine and fasting plasma glucose, plasma level of apelin standard transthoracic echocardiogram, as well as measurement of body mass index, waist circumference, waist hip ratio and waist height ratio. Obesity was defined as body mass index ≥30 kg/m^2, waist circumference≥ 94cm for men and ≥ 80 cm for women, waist height ratio ≥0.5 and waist hip ratio ≥0.85 in females and ≥0.90 in males.

Results: There was no significant difference between obese and non obese patients as regarding Gensini score ,most probably due to small sample size . Plasma apelin level did not show significant difference between groups. Body mass index correlated significantly with total cholesterol (r=0.140, p=0.012) and with LDL-C (r =0.132, p= 0.018) , body mass index was also correlated with plasma apelin level (r=0.232, p= 0.039) , waist circumference correlated significantly with total cholesterol (r = 0.150 , P= 0.007) , waist height ratio correlated significantly with total cholesterol (r = 0.183 , p= 0.001) and with LDL-C (r = 0.140 , p= 0.012)

Conclusion: We concluded in our study that there no difference was found in plasma apelin between obese and non obese patients and no correlation between apelin and Gensini score. Also females was predominant in obese group. There was an increase in cardiovascular risk factors among obese Egyptian patients .

Keywords: Visceral obesity, Apelin, Coronary artery disease

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List of Abbreviations

ACS		Acute coronary syndrom
ADA		American Diabetes Association
Ang II	:	Angiotensin II
APJ	:	Apelin receptors
Apo	:	Apoprotiens
AT1		Angiotensin 1
ATP	:	Adenosin triphosphate
AtRa	:	Alltransretinoic acid
BIA	:	Bioelectrical Impendence analysis
BMI	:	Body mass index
CABG	:	Coronary Artery by pass grafting
CAD	:	Coronary artery disease
CAC	:	Coronary artery calcium
CPAP	:	Continuous positive airway pressure
CKD	:	Chronic kidney disease
CT	:	Computed tomography
CTA	:	Computed tomography angiography
CVD	:	Cardiovascular disease
CVS	:	Cardiovascular stroke
DXA	:	Dual energy X ray absorptimetry
ECG	:	Electrocardiography
ELISA	:	Enzyme linked immunosorbent assay
FEV1	:	Forced expiratory volume in first second
FFA	:	Free fatty acids
FPG	:	Fasing plasma glucose
FRC	:	Functional residual capacity
FVC	:	Forced vital capacity
HDL	:	High density lipoprotiens
HTN	:	Hypertension
IDF	:	International diabetes federation
IL	:	Interleukin

IR	:	Insulin resistance
I/R	:	Ischemia / reperfusion injury
LDL	:	Low density lipoprotien
LVEF	:	Left ventricular ejection fraction
MAP	:	Mean arterial pressure
MCP 1	:	Monocyte chemoattractant protein 1
MI	:	Myocardial infarction
MPTP	:	Mitochondrial Permeability Transition Pore
MRI	:	Magnetic resonance imaging
NHANES	:	National health and nutrition examination survey
NHP	:	National hypertension project
NICE		National Institute for health and care excellence
NIDD	:	Non insulin dependent diabetes mellitus
NO	:	Nitric oxide
NOS	:	Nitric oxide synthase
NYHA	:	NewYork heart association
OSA	:	Obstructive sleep apnea
PAI	:	Plasminogen activator inhibitor
P crti	:	Critical closing pressure
PKC	:	Phosphokinase C
PLC	:	Phospholipase C
PVD	:	Peripheral vascular disease
RAS	:	Renin angiotensin system
RCA	:	Right coronary artery
RISK	:	Reperfusion injury salvage kinase
RV	:	Residual volume
SES	:	Socioeconomic status
SD		Standard Deviation
STEMI	:	ST elevation myocardial Infarction
T1DM	:	Type 1 diabetes mellitus
T2DM	:	Type 2 diabetes mellitus
TLC	:	Total lung capacity

TNF	:	Tumor necrosis factor
TTE	:	Tran thoracic echocardiography
UA	:	Unstable angina
US	:	Ultrasound
VFA	:	Visceral fat adeposity
V/S	:	Visceral / subcutaneous
WAT	:	White adipose tissue
WC	:	Waist circumference
WHR	:	Waist hip ratio
WHO	:	World health organization
WHtR	:	Waist height ratio

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INTRODUCTION

The beneficial impact on cardiovascular morbidity and mortality of favorable trends in population control of classic risk factors such as smoking, hypercholesterolemia, and hypertension may be reversed by the current epidemic of obesity [(1)]. Obesity, in particular abdominal adiposity, is associated with increased risk of cardiovascular disease (CVD) and type 2diabetes mellitus **(**T2DM**)** [(2)].

Recent publications have shown that the overweight and particularly the obese have progressively higher morbidity and mortality[(3)]. The multinational INTERHEART case control study confirmed the importance of obesity, particularly abdominal adiposity, as a potent risk factor for myocardial infarction [(4)].

Abdominal obesity, which reflects central body fat distribution, has been suggested as a better marker of the obesity risk [(5)].

Excess visceral fat is important in the etiology of chronic diseases T2DM, hypertension, coronary artery diseases (CAD) given its association with circulating free fatty acids, insulin resistance (IR), hyperinsulinemia, dyslipidemia, and atherosclerotic inflammatory markers [(6)].

Waist circumference (WC) and the waist hip ratio (WHR)are widely used as indicators of abdominal adiposity in epidemiologic studies. Compared with WHR, WC has been shown to be a better marker of visceral fat [(7)] and correlates more strongly with CVD risk factors [(8)]. WHR has also been shown to be a good predictor of increased risk of T

2DM [9] and CAD [10] which may be due to attributes related to small hip relative to WC. Cross-sectional and prospective studies have found that when WC is taken into account, a larger hip circumference is associated with reduced risk factors for T2DM [11] and CVD [12].

Abdominal obesity is also a significant risk factor for atherosclerosis.

Excessive accumulation of visceral fat is associated with IR and compensatory hyperinsulinemia, which contributes to atherosclerotic progression[13].

CAD is the single leading cause of death in the United States, and accounted for 1 of every 6 deaths in 2009. Approximately 1.2 million people in the United States suffer a new or recurrent heart attack each year, and nearly half (47%) die before they receive emergency services[14].

Apelin is a novel peptide that acts through the apelin receptors (APJ receptor), sharing similarities with the angiotensin II–angiotensin II type 1 receptor pathway. It is one of the adipokines secreted from human adipose tissue. It is a peripheral vasodilator, powerful inotrope and may affect central fluid homeostasis [15]. In obese subjects, plasma apelin is about fivefold higher than it is in lean controls [16].

Most of the adipocytokines secreted by visceral fat reduce the visceral fat volume or normalize the visceral /subcutaneous ratio (V/S ratio), on the contrary, with a change in plasma adipocytokine level and imbalance among them in the body for a long term, it will become a

pathological condition and may contribute to the development of (IR) by various kinds of effects [17] .

Plasma apelin levels are lower in child obesity and pubertal state is an important determinant of plasma apelin levels [18].

Apelin could be considered a 'good' adipokine when considering CVD. It reduces atherogenesis, macrophage inflammation, mean arterial pressure (MAP), cardiomyocyte contractility, atrial fibrillation and heart failure. It is cardioprotective, given that it reduces infarct size in I/R models, delaying mitochondrial permeability transition pore (MPTP) opening. Knockout studies demonstrate that the absence of apelin increases cardiac dysfunction. However, its role in ischemic heart disease and heart failure is not fully understood. The myocardial expression of apelin may differ from plasma levels, the conclusions from which are as yet unclear[19]. Further research is required in delineating its role in the myocardium in different pathologies.