Study of Serum Levels of Cyclophilin A in Patients with Coronary Artery Disease

Thesis

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Rana Mahmoud Sedky

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List of Abbreviations

Abb.	Full term
ACS	*Acute Coronary Syndrome*
AMI	*Acute Myocardial Infarction*
Apo A-1	*Apo-Lipoprotein A-1*
AUC	*Area under Curve*
BMI	*Body Mass Index*
CABG	*Coronary Artery Bypass Graft*
CD147	*Cluster of Differentiation 147*
CK	*Creatine Kinase*
CK-MB	*Creatine Kinase MB Fraction*
CLD	*Cyclophilin-Like Domain*
CMIA	*Chemiluminescent Microparticle Immunoassay*
CMR	*Cardiac Magnetic Resonance*
CRP	*C- Reactive Protein*
CsA	*Cyclosporine A*
CT	*Computed Tomography*
CTA	*Computed Tomography Angiography*
CyPA	*Cyclophilin A*
DALY	*Disability Adjusted Life Years*
DBP	*Diastolic Blood Pressure*
DM	*Diabetes Mellitus*
EC	*Endothelial Cells*
ECG	*Electrocardiography*
eCyPA	*Extracellular Cyclophilin A*
ELISA	*Enzyme Linked Immunosorbent Assay*
EMG	*Exponentially Modified Gaussian*
eNOS	*Endothelial Nitric Oxide Synthase*
EPC	*Endothelial Progenitor Cell*
ER	*Endoplasmic Reticulum*
GC-A	*Guanylate Cyclase A*

List of Abbreviations (Cont...)

Abb.	Full term
HbA_{1c}	*Glycated Hemoglobin*
HBV	*Hepatitis B Virus*
HCV	*Hepatitis C Virus*
HDL-C	*High Density Lipoprotein Cholesterol*
His	*Histidine*
HIV	*Human Immunodeficiency Virus*
HPLC	*High Performance Liquid Chromatography*
HR	*Heart Rate*
HRP	*Horse Radish Peroxidase*
Hs-CRP	*High Sensitive C Reactive Protein*
ICAM	*Intracellular Adhesion Molecule*
iCyPA	*Intracellular Cyclophilin A*
IFN-γ	*Interferon γ*
IL-1β	*Interleukin 1β*
IL_6	*Interleukin 6*
IL-8	*Interleukin 8*
LDL	*Low Density Lipoproteins*
LVEF	*Left Ventricular Ejection Fraction*
Lys	*Lysine*
M1	*Matrix Protein 1*
MAPK	*Mitogen Activated Protein Kinase*
MCP-1	*Monocyte Chemoattractant Protein-1*
MGB	*Minor Groove Binder*
MMP-9	*Matrix Metalloproteinase-9*
NADPH	*Reduced Nicotinamide Adenine Dinucleotide Phosphate*
NFQ	*Nonfluorescent Quencher*
NF-κB	*Nuclear Factor Kappa B*
NO	*Nitric Oxide*

List of Abbreviations (Cont...)

Abb.	Full term
NPV	*Negative Predictive Value*
NSTEMI	*Non ST Elevation Myocardial Infarction*
OD	*Optical Density*
PCI	*Percutaneous Coronary Intervention*
PIT	*Pathological Intimal Thickening*
PPIA	*Peptidyl Prolyl Isomerase A*
PPV	*Positive Predictive Value*
RAAS	*Renin Angiotensin Aldosterone System*
RLUs	*Relative Light Units*
ROC	*Receiver Operating Characteristic Curve*
ROS	*Reactive Oxygen Species*
SAA	*Serum Amyloid A*
SBP	*Systolic Blood Pressure*
SDS	*Sodium Dodecyl Sulphate*
SMC	*Smooth Muscle Cell*
SOD	*Super Oxide Dismutase*
STEMI	*ST Elevation Myocardial Infarction*
TCFA	*Thin Cap Fibro Atheroma*
TNF-α	*Tumour Necrosis Factor – Alpha*
UA	*Unstable Angina*
VCAM-1	*Vascular Cell Adhesion Molecule-1*
VEGF	*Vascular Endothelial Growth Factor*
VSMC	*Vascular Smooth Muscle Cell*
WHO	*World Health Organization*
XO	*Xanthine Oxidase*

ABSTRACT

The study revealed that levels of CypA were significantly higher among studied atherosclerotic CAD patients when compared to the control group ($p<0.01$). Also, patients with zero vessel disease showed significantly higher CyPA levels than control group ($p<0.05$); suggesting the role of this marker in early detection of the atherosclerotic process. Moreover, zero vessel disease patients significantly differed in their CyPA levels compared to 1, 2, and 3 vessel disease patients; ($p<0.05$).

On the other hand, the differentiation between more advanced conditions of the CAD, wasn't revealed in our study. There was no significant difference in the CyPA levels among the patients' groups starting from 1 vessel disease till the 3 vessel disease.

Keywords: Sodium Dodecyl Sulphate - Vascular Smooth Muscle Cell - Systolic Blood Pressure

INTRODUCTION

Coronary artery disease is a complex chronic inflammatory disease, characterized by remodeling and narrowing of the coronary arteries supplying oxygen to the heart. It can have various clinical manifestations, including stable angina, acute coronary syndrome, and sudden cardiac death ***(DeGoma et al., 2012).*** It is the leading cause of death worldwide being responsible for approximately one-third of all deaths in individuals older than 35 years ***(Hanson et al., 2013).***

Coronary Artery Disease has a complex etio-pathogenesis and a multi-factorial origin related to environmental factors, such as diet, smoking, and physical activity. However, genetic factors have been claimed to modulate risk of the disease ***(Sayols-Baixeras et al., 2014).*** Ideally, recognizing those at risk for CAD would help identify such individuals and decrease the incidence of this ominous presentation ***(Ibrahim et al., 2012).***

It has been reported that the plasma levels of high-sensitivity C-reactive protein (hs-CRP), brain natriuretic peptide (BNP), D-dimer, and fibrinogen can predict the occurrence of cardiovascular events and progression. However, the plasma levels of these biomarkers are increased in inflammatory diseases, in general, in addition to arteriosclerotic diseases. Thus, the search for a useful biomarker that can effectively predict the risk of future progression to more serious cardiovascular events still remains to be developed ***(Ohtsuki et al., 2017).***

Scoring system that predicts the risk of death and MI "GRACE" score (Global Registry of Acute Coronary Events) has been established. The components of the GRACE risk score (ranging from 2 to 372) are age, heart rate, systolic blood pressure, Killip class (classification of heart failure), cardiac arrest at admission, serum creatinine, ST-segment deviation and cardiac biomarker status. According to this score, patients can be grouped into 3 tertiles of death risk; low, intermediate and high ***(Khalil et al., 2009).***

Cyclophilin A (CypA) is a protein that is secreted from vascular smooth muscle cells in response to reactive oxygen species ***(Taguchi et al., 2013).*** It has been claimed that CypA plays a role in the pathogenesis of various cardiovascular diseases such as vascular stenosis. Moreover, it is suggested that CypA plays a role in later stages of atherosclerosis and plaque rupture. However, little information has addressed the potential relationship between CypA and severity in patients with CAD ***(Satoh et al., 2013).***

Therefore, researches are designed to investigate the relation between serum CypA concentration and the coronary complex stenosis morphology in patients with CAD ***(Yan et al., 2012)***.

AIM OF THE WORK

The present study aims to assess severity of CAD and predict future cardiovascular events through:

A. Correlating levels of serum CyPA with coronary angiography results.

B. Correlating levels of serum CyPA with GRACE score.