بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Evaluation of Cyclophilin A in Type II Diabetic Patients with Coronary Artery Disease

Submitted By

Hala Fayez Ebrahim Taha

B.Sc. (2010) in Biochemistry
Diploma of Analytical Biochemistry (2014)
Faculty of Science, Ain Shams University

For the Fulfillment of Master Degree in Biochemistry

Under supervision

Prof. Dr. Fatma F. Abdel Hamid

Professor of Biochemistry
Biochemistry Department
Faculty of Science
Ain Shams University

Dr. Ahmed F. Soliman

Lecturer of Biochemistry
Biochemistry Department
Faculty of Science
Ain Shams University

Biochemistry Department
Faculty of Science
Ain Shams University
2020

بسم الله الرحمن الرحيم

(قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ العَلِيمُ الحَكِيمُ)

صدق الله العظيم
البقرة - الآية 32

Ain Shams University
Faculty of Science

Name	: Hala Fayez Ebrahim
Scientific Degree	: B.Sc. in Biochemistry
Department	: Biochemistry
Faculty	: Science
University	: Ain Shams
Graduation Year	: 2010

I declare that this thesis has been composed by myself and the work herein has not been submitted for a degree at this or any other university.

Hala Fayez Ebrahim

Acknowledgment

First of all, I offer thanks always to ALLAH, for his great care and guidance in every step of my life and for giving me the ability to complete this work and who made all things possible.

It was a great pleasure for me to express my deep gratitude and appreciation to ***Prof. Dr. Fatma F. Abdel Hamid,*** *Professor of Biochemistry, Biochemistry Department, Faculty of Science, Ain Shams University, for her continuous guidance, advice and supervision and sacrificing a lot of her precious time to revise each and every step of this study. It is hard for me to find the appropriate words that would do her favors.*

I would like to express my deep gratitude to ***Dr. Ahmed F. Soliman,*** *Lecturer of Biochemistry, Biochemistry Department, Faculty of Science, Ain Shams University, for his keen supervision and continuous assistance and constant support and encouragement are much appreciated. I am grateful in every possible way for his wise opinions and critical comments throughout the whole study and work.*

I wish also to express my deep gratitude to ***Dr. Mohamed A. Haykal*** *at Cardiovascular and Ultrasonography Unit, Research Institute of Ophthalmology for his help in the collection of the study samples.*

I wish also to express my thanks to all my family for their endless support and unyielding faith in me and for their tolerance of my absence, physically and emotionally stress many, many thanks. The completion of this thesis would have never been conceivable without their fervent motivation.

Hala F. Ebrahim

Abstract

Objectives: Data about the circulating levels of cyclophilin A (CyPA) and matrix metalloproteinase-9 (MMP-9) in stable coronary artery disease (CAD) is contradictory. Moreover, their relationship in this disease is not established yet. Thus, this study was designed to assess the relationship between the circulating levels of CyPA and MMP-9 in CAD patients with and without type 2 diabetes mellitus (T2DM).

Methods: Serum levels of CyPA, MMP-9, and high sensitive C-reactive protein (hsCRP) along with fasting blood glucose, glycated hemoglobin, serum lipids, and the anthropometric parameters were measured in one hundred and twenty participants who were divided equally into four groups (I) normal controls, (II) T2DM patients, (III) stable CAD patients with T2DM, and (IV) stable CAD patients without T2DM.

Results: Levels of CyPA and MMP-9 were significantly elevated in sera of CAD patients with and without T2DM compared to normal controls and T2DM patients. In multiple linear regression models, only CyPA was observed in the final model where it explained the 24.9% variability of MMP-9. Additionally, high circulating levels of CyPA and MMP-9 were associated with an increased risk of developing stable CAD. Finally, the diagnostic efficacy of CyPA and MMP-9 to discriminate stable CAD patients with and without T2DM from subjects without CAD was found to be higher than that of hsCRP.

Conclusion: Serum level of CyPA might be a determinant factor of MMP-9 level, both may contribute to the pathogenesis of stable CAD, and they appear to be valuable diagnostic biomarkers of stable CAD with and without T2DM.

Contents

List of Tables

List of Figures

List of Abbreviations

ADA:	American diabetes association
AGEs:	Advanced glycation end-products
AMI:	Acute myocardial infarction
BMI:	Body mass index
BNP:	Brain natriuretic peptide
CAD:	Coronary artery disease
CD:	Cluster of differentiation
CRP:	C-reactive protein
CVD:	Cardiovascular disease
CWC27:	Spliceosome-associated protein CWC27 homolog
CyPA:	Cyclophilin A
DM:	Diabetes mellitus
EC:	Endothelial cells
ECM:	Extracellular matrix
ELISA:	Enzyme linked immunosorbent assay
EMMPRIN:	Extracellular matrix metalloproteinase inducer
eNOS:	Endothelial nitric oxide synthase
ERK:	Extracellular signal-regulated kinase
FBG:	Fasting blood glugose
FFAs:	Free fatty acids
GADAs:	Glutamate decarboxylase autoantibodies
GAPDH:	Glyceraldehyde-3-phosphate dehydrogenase
GBM:	Glomerular basement membrane
GFR:	Glomerular filtration rate
HbA1c:	Glycated hemoglobin
HDL-C:	High-density lipoprotein cholesterol
HPLC:	High performance liquid chromatography
hsCRP:	high-sensitivity CRP
ICAM-1:	Intracellular adhesion molecule 1
IDF:	International diabetes federation
IFG:	Impaired fasting glucose
IGT:	Impaired glucose intolerance

IL:	Interleukin
KLF2:	Kruppel-like factor 2
MAPK:	Mitogen-activated protein kinase
MARD:	*Mild age-related diabetes*
MMP:	Matrix metalloproteinase
MOD:	Mild obesity-related diabetes
MPAs:	Monocyte-platelet aggregates
MT-MMPs:	Membrane-type MMPs
NF-κB:	Nuclear factor-kabba B
oxLDL:	Oxidized LDL
PKC:	Protein kinase C
PMNs:	Polymorphonuclear neutrophils
PPI:	Peptidyl prolyl isomerase
PPIL4:	Peptidyl prolyl isomerase-like 4
PPWD1:	Peptidyl prolyl isomerase WD repeat-containing protein 1
RAGEs:	Receptors for AGEs
RANBP2:	RAN binding protein 2
RANBP2:	RAN binding protein 2
ROS:	Reactive oxygen species
SAID:	Severe autoimmune diabetes
sdLDL:	Small dense low-density lipoprotein
SIDD:	Severe insulin-deficient diabetes
SIRD:	Severe insulin-resistant diabetes
T1DM:	Type 1 diabetes mellitus
T2DM:	Type 2 diabetes mellitus
TGF-α:	Transforming growth factor-alpha
TIMP:	Tissue inhibitor of matrix metalloproteinase
TNF-*α*:	Tumor necrosis factor-alpha
VCAM-1:	Vascular cell adhesion molecule 1
VLDL:	Very low-density lipoprotein
VSMC:	Vascular smooth muscle cells