

Pattern of Atherosclerosis in Extracranial and Intracranial Vessels in Non-Stroke Diabetic Patients with Atherosclerotic Coronary Artery Disease

Thesis

submitted For Partial Fulfillment of Master degree of Cardiology

By

Mohamed Mostafa Farouk Mohamed

Under Supervision of

Professor Doctor/ Mohamed Awad Taher

Professor of Cardiology
Ain Shams University

Assistant Professor Doctor/ Azza ABD EL Naser ABD EL Aziz

Assistant Professor of Neuropsychiatry
Ain Shams University

Doctor/ Ahmed Mohamed Onsy Ibrahim Atia

Lecturer of Cardiology Ain Shams University

Faculty of Medicine-Ain Shams University

Cardiology Department

2009

Acknowledgment

First and foremost, I thank *God* for helping and guiding me in accomplishing this work.

I would like to express my sincere gratitude to *Professor Dr. Mohamed Awad Taher*, the great Professor of Cardiology, Ain Shams University, firstly for giving me the honor to be his student.

I must extend my warmest gratitude to *Dr. Azza ABD EL Naser ABD EL Aziz*, Assistant Professor of Neuropsychiatry, Ain Shams University, for her great help and faithful advice.

Many great thanks for *Dr. Ahmed Mohamed Onsy;* lecturer of cardiology, Ain Shams University, whom fruitful thinking was behind the progress of this work.

Never to forget those whom effort was a corner stone to complete this work, *Dr Kareem Ahmed Abd-Eltawaab;* Radio-diagnosis department, *Dr Hossam EL Dein Mahmoud;* Assistant Lecturer of Neuropsychiatry and *Dr. Yehia Makkeyah;* Assistant Lecturer of Nephrology (for statistics).

Last but definitely not the least, I would like to thank *my family* for always being there. To them I owe my life.

LIST OF CONTENTS

	Acknowledgment	
	List of contents	i
>	List of tables	ii
	List of figures	V
	List of abbreviations	viii
	Introduction	1
	Aim of the work	3
	Review of literature:	
	■ Chapter 1: Diabetes mellitus	4
	■ Chapter 2: Atherosclerosis as a systemic disease	21
	■ Chapter 3: Carotid ultrasonography	40
	Chapter 4: Role of TCD in assessment of intracranic vessels	
	Patients and methods	92
	Results	105
	Discussion	134
	Limitations	140
	Conclusions	141
	Recommendations	142
	English Summary	143
	References	146
	Master table	167

LIST OF TABLES

Table 1: Classification of diabetes mellitus
Table 2: Virchow's Triad of Thrombogenicity 34
Table 3: Identifying features of external carotid arteries 50
Table 4: Normal values of PI for ACA, MCA& Extracranial ICA
Table 5: Effects of Different Physiological States on TCD Flow Velocity
Table 6: Data used for diagnosis of diabetic patients
Table 8: Normal values of mean blood velocity for ACA, MCA, PCA, VA and BA 103
Table 9: Distribution of demographic data and risk factors in the study population112/113 Table 10: Pattern of IHD in the study population15
Table 11: Distribution of extracranial atherosclerosis among the study population
Table 12: Data of carotid duplex in the study population 116
Table 13: Distribution of intracranial (anterior and posterior circulation) atherosclerosis among the study population 117
Table 14: Data of TCD in the study population 118

carotid atherosclerosis
Table 16: Relationship between age and the carotid IMT 121
Table 17: Relationship between the age and the pattern of atherosclerosis in the intracranial vessels
Table 18: Relationship between the waist circumference and the extracranial atherosclerosis
Table 21: Relationship between glycemic control (HbA1c) and extracranial atherosclerosis
Table 22: Relationship between glycemic control (HbA1c) and the carotid IMT
Table 23: Relationship between glycemic control (HbA1c) and intracranial atherosclerosis
Table 24: Relationship between number of coronaries stenosed >50% and the extacranial atherosclerosis
Table 25: Relationship between number of coronaries stenosed >50% and the carotid IMT
Table 26: Relationship between number of coronaries stenosed >50% and the right carotid largest plaque homogeneity 127
Table 27: Relationship between number of coronaries stenosed >50% and the intacranial atherosclerosis

List of tables

: Relationship erosis	•	•	
: Relationship	•	•	
: Relationship erosis	•	•	
Relationship		05	

LIST OF FIGURES

Figure 1 : Shows the clinicopathologic correlation of asymptomatic atherosclerosis leading to symptomatic atherothrombosis
Figure 2: Shows the relation between hyperlipidemia and endothelial dysfunction
Figure 3: Shows the role of nitric oxide dysregulation in increased lipid accumulation in the vessel wall
Figure 4: Shows the duplex features of normal carotid artery
Figure 5: Shows that the internal carotid artery (ICA) has high diastolic flow
Figure 6: Shows that the external carotid artery (ECA) shows low velocity flow in diastole
Figure 7: Shows a homogeneous plaque in the proximal right ICA
Figure 8: Shows a heterogeneous plaque in the proximal right ICA57
Figure 9: Shows the steps of FCT measurement
Figure 10: Shows that IVUS can help identification of plaque morphology and structure

Figure 11: shows the method used in the NASCET study to assess the degree of carotid stenosis70
Figure 12: Shows the method used in the ECST study to assess the degree of carotid stenosis
Figure 13 : Shows the TCD probe positions over different acoustic windows of the skull
Figure 14: Shows the different regions of the Transtemporal window,77
Figure 15: Shows the normal TCD Waveform of Middle Cerebral Artery,87
Figure 16: Shows the distribution of different age groups in study population,107
Figure 17: Shows the distribution of smoking in study population,107
Figure 18: Shows the distribution of HTN, WC and lipid profile in study population,110
Figure 19: Shows time of diagnosis or discovery of DM in study population,110
Figure 20: Shows Type of treatment of DM in study population,111
Figure 21: Shows the degree of glycemic control (measured by HbA1c) in study population112
Figure 22 : Shows the Distribution of extracranial atherosclerosis in study population,117

Figure 23: Shows the Distribution of intracranial
atherosclerosis in study population119
Figure 24: Shows the relationship between different age groups and pattern of atherosclerosis in the left carotid system
Figure 25: Shows the relationship between age and right carotid IMT
Figure 26: Shows the relationship between age and leftt carotid IMT
Figure 27: Shows the relationship between waist circumference and pattern of posterior circulation atherosclerosis
Figure 28: Shows the relation between number of coronaries stenosed >50% and right largest carotid plaque homogeneity
Figure 29: Shows the relation between serum TGs level and pattern of atherosclerosis in right carotid system
Figure 30: Shows the relation between serum TGs and right vertebral artery (VA) pulsatility index (PI)

LIST OF ABBREVIATIONS

2hPPG	Two hours Postprandial Plasma Glucose
ABP	Arterial blood Pressure
ACA	Anterior Cerebral Artery
ACC	American Colleague Of Cardiology
ACoA	Anterior Communicating Artery
ACS	Acute Coronary Syndrome
АНА	American Heart Association
ANOVA	Analysis Of Variants
Apo	Apoproteins
ASUSH	Ain-shams University Specialized Hospital
AVMs	Arterio-Venous malformations
BA	Basilar Artery
CA	Coronary Angiography
CAMs	Cell Adhesion Molecules
CBF	Cerebral Blood Flow

CBFV	Cerebral Blood Flow Velocity
CCA	Common Carotid Artery
CCU	Coronary Care Unit
CDFI	Color Doppler flow imaging
CDU	Color Doppler Ultrasound
C-GMP	Guanidine Monophosphate
CHD	Coronary Heart Disease
CRP	C-Reactive Protein
CSA	Chronic Stable Angina
CSF	Cerebrospinal Fluid
СТ	Computed Tomography
СТ	Computed Tomography
CVS	Cerebrovascular stroke
DBP	Diastolic Arterial blood Pressure
DM	Diabetes Mellitus
ECA	External Carotid Artery

ECG	Electrocardiogram
ЕСНО	Echocardiography
ECST	European Carotid Surgery Trial
EDV	End Diastolic Flow Velocity
eNOS	Endothelial nitrous oxide synthetase
ESC	European Society Of Cardiology
ET	Endothelin
FBG	Fasting Blood Glucose
FC	Fibrous Cap
FCT	Fibrous Cap Thickness
FPG	Fasting Plasma Glucose
FV	Flow Velocity
Gluts	Glucose transporters
HbA1c	Glycosylated hemoglobin
HDL	High density lipoproteins
НРЕТЕ	Hydroperoxyeicosatetraenoic Acid

HPODE	Hydroperoxyoctadecadienoic Acid
HTN	Hypertension
HV	Haematocrite Value
ICAS	Intracranial Atherosclerosis
ICE	Internal Carotid Artery
IDDM	Insulin Dependent Diabetes Mellitus
IFG	Impaired Fasting Glycemia
IHD	Ischemic Heart Disease
ILD	Intermediate Density lipoproteins
IMT	Intima-Media Thickness
IVUS	Intravascular Ultrasonography
LDL	Low density lipoproteins
LDLr	Low density lipoproteins receptors
Lp(a)	Lipoprotein (a)
MCA	Middle Cerebral Artery
МСР	Monocyte Chemotactic Protein

M-CSF	Monocyte Colony Stimulating Factor
MFV	Mean Flow velocity
MMP	Matrix Metalloproteinases
MRA	Magnetic Resonance Angiography
n	number
NASCET	American Symptomatic Carotid Endarterectomy Trial
NFKB	Nuclear Factor Kappa B
NIDDM	Non Insulin Dependent Diabetes Mellitus
NO	Nitric Oxide
NSTEMI	Non ST Segment Elevation Myocardial Infarction
OA	Ophthalmic Artery
P1	The First Branch Of Posterior Cerebral Artery
PaCO2	Carbon Dioxide Tension In The Blood
PAI	Plasminogen Activator Inhibitor
PCA	Posterior Cerebral Artery
PCoA	Posterior Comunicating Artery

PDS	Power Doppler Ultrasound
PGI2	Prostaglandin I2
PI	Pulsatility Index
PON	Paraoxonase
PSV/PV	Peak Systolic Flow Velocity
PVI	Plaque Volume Index
SBP	Systolic Arterial blood Pressure
SD	Standard Deviation
SMC	Smooth Muscle Cell
SRA	Class A scavenger receptor
SRB	Class B scavenger receptor
STEMI	ST Segment Elevation Myocardial Infarction
ТС	Total Cholesterol
TCD	Transcranial Doppler
TCFA	Thin Cap Fibroatheroma
TFPI	Tissue Factor Pathway Inhibitor