Short term impact of diabetes and its comorbidities in patients undergoing coronary artery bypass graft surgery

Thesis submitted for the fulfillment of master degree in cardiology

By Khaled Mohamed Abdullah Aladib , M.B.B.Ch,

Supervised by **Prof. Dr. Mohamed Zaki El Ramly**

Professor of cardiology, Faculty of Medicine- Cairo University

Dr. Azza Abdel Moniem Farrag

Assistant Professor of cardiology, Faculty of Medicine- Cairo University

Dr. Sameh Ahmed Salama

Assistant Professor of cardiology, Faculty of Medicine- Cairo University

> Faculty of Medicine Cairo university 2010

Acknowledgement

First and foremost thanks are to **GOD** the most beneficent kind and merciful.

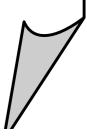
I am gratefully honored to express my sincere appreciation to **Prof. Dr. Mohamed Zaki El Ramly,** Professor of cardiology, Faculty of Medicine-Cairo University for his supervision and guidance.

I would like to express my deep gratitude to **Dr. Azza Abdel Moniem Farrag** Assistant Professor of cardiology, Faculty of Medicine- Cairo University for her continuous help, active support and guidance throughout every step in this work which without her advices this work would not be completed.

I would like to express my sincere gratitude to **Dr. Sameh Ahmed Salama** Assistant Professor of cardiology, Faculty of Medicine- Cairo University for his continuous guidance and supervision in criticizing and correcting the whole thesis and encouragement which he always offered willingly. To him I extend my sincere thanks.

Words will never be able to express my deepest gratitude to **my Mother**, **brothers and Wife**, those who helped me during preparation of this study.

I dedicate this work to **my father** who was credited in my life and encouraged me in my studies and I joined the Faculty of Medicine.



Abstract

Short term impact of diabetes and its comorbidities in patients undergoing coronary artery bypass graft surgery

Background: Diabetes mellitus (DM) is a major risk factor for cardiovascular disease. It affects about 15% of Middle East population. Patients with DM are known to be a high risk group for early morbidity and mortality following coronary artery bypass grafting (CABG). The purpose of this study was to identify the impact of DM and its related co-morbidities on short-term morbidity and mortality following CABG, and if there any outcome differences between diabetic and non-diabetic patients.

Methods: Data were prospectively collected from 354 patients scheduled for CABG in two tertiary centers during a period of 3 months. Mean age was 56±9 years, 205 (57.9%) were diabetics. All patients underwent an elective operation.

Results: Diabetics were significantly more hypertensive (74.6% vs. 54.4%, p= 0.000), had a history of cerebrovascular stroke (CVS) (7.3% vs. 1.3%, p= 0.01) and congestive heart failure (12.7% vs. 5.4%, p= 0.027). They were less smokers (59.5% vs. 79.9%, p= 0.000) but had higher body mass index (30.2 \pm 5.6 vs. 28.2 \pm 4.9, p= 0.001). Age was comparable and female gender was more in the diabetic group (p= 0.000). Despite that diabetics had a higher Euroscore (2.4 \pm 1.5 vs. 2.0 \pm 1.3, p= 0.002), no significant differences were found as regards post-operative complications. Post operative acute renal failure, respiratory failure, CVS, acute myocardial infarction, bleeding, unplanned re-operation or sternal wound infection was all comparable for both groups. Hospital mortality was not statistically significant (4.9% vs. 4%, p= 0.799%) for diabetic and non-diabetic group respectively.

Conclusion: Diabetic patients although had higher pre-operative morbidities, they

yet had comparable post-operative morbidity and mortality. Diabetes should not be

considered as a risk factor in the outcome of patients undergoing CABG.

Key Words: CABG- Diabetes – Bypass – Coronary artery

LIST OF CONTENT

List	Page
List of Tables	I
List of Figures	III
List of Abbreviations	IV
List of Abbreviations for master sheet	VIII
Introduction	1
Aim of work	3
Review of Literature	4
Chapter1:	4
 Coronary artery disease and diabetes mellitus. 	
Chapter 2 :	
 Medical treatment of coronary artery disease in diabetic patients. 	19
Chapter 3:	
 Coronary artery bypass grafting and diabetes mellitus. 	35
Methodology	56
Results	73
Master Sheet	71
Discussion	112
Summary	120
Conclusion	123
References	124
Arabic Summary	1

<u>List of Tables</u>

Table No.	Tilt	Page
Table 1	Potential Impact of Insulin Resistance and	13
	Diabetes on Thrombosis	
Table 2	Potential Impact of Insulin Resistance and	13
	Diabetes on Fibrinolysis	
Table 3	Prevention of Thrombotic Events by	20
	Inhibitors of Platelet Aggregation	
Table 4	EuroSCORE	42
Table 5	EuroSCORE	43,58
Table 6	Clinical outcomes of coronary artery	44
	bypass surgery	
Table 7	Demographic and Clinical characteristics	63
	of the whole studied population	
Table 8	Echocardiographic characteristic of all	65
	patients	
Table 9	angiographic characteristic of all patients	65
Table 10	Operative characteristic of the whole	66
	studied population	
Table 11	Post operative characteristics of the whole	66
	studied population	
Table 12	Demographic and Clinical characteristics	69
	of the two studied groups	

Table 13	Echocardiographic characteristic of both	70
	studied groups	
Table 14	Angiographic characteristic of both	70
	studied groups	
Table 15	operative characteristic of both groups	71
Table 16	postoperative morbidities and mortality of	72
	the both studied groups	

List of Figures

Figure No.	Tilt	Page
Figure 1	Demographic and Clinical characteristics of the whole studied population	64
Figure 2	Post operative characteristics of the whole studied population	67
Figure 3	postoperative morbidities of both studied groups	72

List of Abbreviations

Abbreviation	Meaning
ABCD	Appropriate Blood Pressure Control in Diabetes
ACE	Angiotensin converting enzyme
ACS	Acute coronary syndrome
ADP	Adenosine diphosphate
AGE	Advanced glycation end products
AHA	American Heart Association
ANOVA	Analysis of variance
AP-1	Activator protein-1
ApoA-I	Apolipoprotein A-I
АроВ	Apolipoprotein B
AT II	Angiotensin I
BARI	Bypass Angioplasty Revascularization Investigation
BITA	Bilateral Internal thoracic arteries
BMS	Bare metal stents
BMI	Body Mass Index
CA	Coronary Angiography
CABG	Coronary Artery Bypass Grafting
CAC	coronary artery calcification
CAD	Coronary artery disease
cAMP	Cyclic adenosine monophosphate
CAPRIE trial	clopidogrel versus aspirin in patients at risk of ischemic
	events
CASS	the Coronary Artery Surgery Study
cGMP	Cyclic guanosine monophosphate.
CCS	Canadian Cardiovascular Society class
CHD	Coronary heart disease
CHF	Congestive heart failure
CI	Confidence Interval
CO	Cardiac output
COPD	Chronic obstructive pulmonary disease
СРВ	Cardiopulmonary bypass
CVA	Cerebrovascular Accidents

CVD	Cardiovascular disease
CVS	Cerebrovascular system
DCCT	Diabetes Control and Complications Trial
DKA	Diabetic Ketoacidosis
DM	Diabetes mellitus
DRS	Diabetic Retinopathy Study
EBCT	Electron beam computed tomography
ECM	Extracellular matrix
ED	Emergency department
EDV	End diastolic volume
EF	Ejection Fraction
eNOS	Endothelial nitric oxide synthase
EPIC	The Evaluation of c7E3 for Prevention of Ischemic
	Complications
ESPRIT	Enhanced Suppression of the Platelet Ilb/Illa Receptor with
	Integrilin Therapy
ESRD	End stage renal disease
ESV	End systolic volume
ET-1	Endothelin-1
ETDRS	Early Treatment Diabetic Retinopathy Study
EuroSCORE	European System for Cardiac Operative Risk Evaluation
FEV1	Forced expiratory volume in 1 second
FFA	Free fatty acid
FPA	Fibrinopeptide A
FPG	Fasting plasma glucose
FVC	Forced vital capacity
GIK	Glucose-Insulin-Potassium
GP	Glycoproteins
HBA1C	Hemoglobin A1c
HERS trial	The Heart and Estrogen Replacement Study trial.
HDL	High-density lipoprotein
HMG-CoA	3-hydroxy-3-methylgluntaryl-coenzyme A
HOPE trial	Heart Outcomes Prevention Evaluation trial
HOT trial	The Hypertension Optimal Treatment trial

IABP	Intra-aortic balloon pump
ICAM-1	Intracellular adhesion molecule
ICM	Ischemic Cardiomyopathy
ICU	Intensive care unit
IDDM	Insulin Dependent Diabetes Mellitus
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IL-1	Interleukin-1
IMA	Internal mammary artery
ITA	Internal thoracic artery
IVUS	Intravascular ultrasonography
LAD	Left anterior descending artery
LCX	Left circumflex artery
LDL	Low-density lipoprotein
LIFE trial	The Losartan Intervention for Endpoint Reduction trial
LIMA	Left internal mammary artery
LOS	Length of stay
LRC	the Lipid Research Clinics
MCE	Myocardial contrast echocardiography
MI	Myocardial infarction
MIBG	Metaiodobenzylguanidine
MIDCAB	Minimally invasive direct coronary artery bypass
MCP-1	Monocyte chemoattractant protein-1
MMPs	Matrix metalloproteinases
MRI	Magnatic resonance imaging
MRFIT	The Multiple Risk Factor Intervention Trial (MRFIT)
NADPH	Nicotinamide adenine dinucleotide phosphate
NIDDM	Non Insulin Dependent Diabetes Mellitus
NO	Nitric oxide
NPDR	Non Proliferative Diabetic Retinopathy
NSTEMI	Non ST Elevation Myocardial Infarction
OASIS	the Organization to Assess Strategies for Ischemic
	Syndromes Registry
OGTT	Oral glucose tolerance test
OPCAB	Off-pump coronary artery bypass
OR	Odds Ratio

PAI-1	Plasminogen activator inhibitor type-1
PCI	Percutaneous Coronary Intervention
PDR	Proliferative diabetic retinopathy
PES	Paclitaxel-eluting stents
PET	Positron emission tomography
PKC	Protein kinase C
PRD	Postoperative renal dysfunction
PTCA	Percutaneous transluminal coronary angioplasty
PVD	Peripheral vascular disease
RAGE	Receptor for advanced glycation end products
RCA	Right Coronary artery
RF	Renal Failure
RI	Renal Impairment
RIMA	Right internal mammary artery
ROS	Reactive oxygen species
ROSETTA-	Routine versus Selective Exercise Treadmill Testing after
CABG	Coronary Artery Bypass Grafting
SD	Standard deviation
SES	Sirolimus-eluting stents
SMC	Smooth muscle cells
STEMI	ST Elevation Myocardial Infarction
STS	Society of Thoracic Surgeons
SVG	Saphenous vein graft
SVD	Single-vessel disease
TIA	Transient Ischemic Attacks
TLR	Target lesion revascularization
t-PA	Tissue-type plasminogen activator
TRACE	The Trandolapril Cardiac Evaluation study
UA	Unstable Angina
UKPDS	The United Kingdom Prospective Diabetes Study
STS	Society of Thoracic Surgeons
VCAM-1	Vascular cell adhesion molecule
VSMC	Vascular smooth muscle cell
WHO	World Health Organization
·	

List of Abbreviations for master sheet

A	Age
G	Gender
BW	Body weight
Н	Height
BMI	Body mass index
D	Diabetes
W/H	Waist/hip ratio
T.D	Type of diabetes
ttt of D	Treatment of diabetes
du	duration
FH.DM	family history of DM
HTN	Hypertension
S	Smoking
CKD	Chronic kidney disease
CVS	Cerebrovascular stroke
COPD	Chronic obstructive pulmonary disease
PVD	Peripheral vascular disease
CHF	Congestive heart failure
Dysl	Dyslipidemia
Chol	Cholesterol
TGs	Triglycerides
FBS	Fasting blood sugar
Cr	Creatinine
LE	Logistic EuroSCORE
LVEDD	Left ventricular end diastolic dimension
LVESD	Left ventricular end systolic dimension
EF	Ejection fraction
RWMSI	Regional wall motion score index
LMA	Left main artery
VD	Vessels disease
N.P	Number of plaque
T.CABG	Type of coronary artery bypass grafting surgery
VB	Number of vessel bypassed
IMA	Internal mammary artery
RF	Renal failure
Resp F	Respiratory failure

ST	Stroke
MI	Myocardial infarction
AF	Atrial fibrillation
URO	Unplanned re-operation
BRR	Bleeding requiring re-exploration
DSW	Deep sternal wound
LS	Length of stay in ICU
M	mortality
Но	Hospital

INTRODUCTION

Diabetes and its related complications and comorbidites are powerful risk factors for cardiovascular disease. The incidence of diabetes is increasing markedly and the World Health Organization estimates that by 2025 there will be 300 million patients with diabetes (5.4 % of the world population).¹

Patients with diabetes constitute a high risk group for early cardiovascular surgical morbidity and mortality. They also account for up to 38% of patients undergoing cardiac procedures, especially coronary revascularization.^{2,3} There is considerable information on preoperative morbidity and mortality in patients with diabetes after coronary artery bypass grafting (CABG) in which poor early outcome and higher in-hospital morbidity and mortality have been demonstrated compared with non diabetic patients.^{4,5,6}

Frequently related comorbidities associated with diabetes, including chronic kidney disease (CKD), peripheral vascular disease (PVD), and left ventricular dysfunction (LVD) can also impact on short term survival in patients undergoing CABG whether diabetic or not. Although CABG surgery has generally become the preferred procedure for initial revascularization in diabetic patients with multivessel disease, it is not without risk. Several studies have examined the role of diabetes and outcomes in CABG patients and the results have been varied. In a study reported by Thouroni et al, mortality in diabetic patients was significantly higher compared to non-diabetic patients with a direct impact of diabetes on early post-operative outcome. More recently, two studies have suggested an improved outcome in diabetic patients and have raised question regarding the potential influence of this disease on early operative results.