

PROSPECTIVE STUDY OF PREDICTORS OF  
MORBIDITY AND MORTALITY IN DIABETIC  
VERSUS NON DIABETIC PATIENTS UNDERGOING  
ELECTIVE PCI TO MULTIVESSEL DISEASE AT  
6<sup>TH</sup> MONTH FOLLOW UP

**Essay**

Thesis submitted for the partial fulfillment of master degree

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**2010**

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## **List of Abbreviations**

<b>CVD:</b>	Cardiovascular disease
<b>NHLBI:</b>	National Heart, Lung, and Blood Institute
<b>CAD:</b>	Coronary artery disease
<b>CHD:</b>	coronary heart disease
<b>ACCF:</b>	American College of Cardiology Foundation
<b>SCAI:</b>	Society for Cardiovascular Angiography and Interventions
<b>ACC:</b>	American Colleague of Cardiology
<b>AHA:</b>	American Heart Association
<b>LVEF:</b>	Left Ventricular Ejection Fraction
<b>LV:</b>	Left Ventricle
<b>MACE:</b>	Major adverse cardiac events
<b>MI:</b>	Myocardial infarction
<b>UA/NSTEMI:</b>	Unstable angina/Non ST Elevation Myocardial Infarction
<b>STEMI:</b>	ST Elevation Myocardial Infarction
<b>LAD:</b>	Left Anterior Descending artery
<b>CHF:</b>	Congestive heart failure
<b>PCI:</b>	Percutaneous coronary intervention
<b>PTCA:</b>	Percutaneous transluminal coronary angioplasty

<b>ACS:</b>	Acute coronary syndrome
<b>CABG:</b>	Coronary artery bypass grafting
<b>IVUS:</b>	Intra vascular ultrasound
<b>BMS:</b>	Bare metal stents
<b>DES:</b>	Drug-eluting stents
<b>RCT:</b>	Randomized controlled trials
<b>FDA:</b>	Food and drug administration
<b>TVR:</b>	Target vessel revascularization
<b>TLR:</b>	Target lesion revascularization
<b>cTn:</b>	Troponin cardiac
<b>PTFE:</b>	Polytetrafluoroethylene
<b>TIA:</b>	Transient ischemic attack
<b>VT:</b>	Ventricular tachycardia
<b>VF:</b>	Ventricular fibrillation
<b>TIMI:</b>	Thrombolysis in myocardial infarction
<b>PAD:</b>	Peripheral arterial disease

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First of All Thanks To **ALLAH**

I would like to express my gratitude to **Prof. Dr. Mahmoud Elsherbeny Abd Elrazek**, Professor of Cardiology, and **Dr. Sherif Samir Elzahwy**, assistant professor of cardiology, Faculty of Medicine, Ain Shams University for their guidance & advice throughout this work, and for their participation and cooperation. They have an active role in this thesis.

Special thanks & deepest gratitude to **Dr. Ahmed Shawky Elserafy**, lecturer of Cardiology, Faculty of Medicine, Ain Shams University, for his great support & guidance. Without his generous encouragement & witty supervision, this work would have never been within hands

Words can not describe my gratitude & indebtedness to my **Mother, Father** and to my great lovely **Wife** who supported me with love & care throughout the hard times.

***Ahmed Sobhi Ashoor***

# Introduction

Patient with DM are known to have a higher incidence of mortality and cardiovascular disease compared with non diabetic patient<sup>(1)</sup>. Insulin requiring diabetics are especially more susceptible to adverse cardiac events<sup>(2)</sup>. Major reasons are the more diffuse and accelerated form of atherosclerosis accompanied by longer lesions length, smaller vessel size and greater plaque burden<sup>(3)</sup>.

Stents are currently used in the overwhelming majority of percutaneous coronary interventions due to the success in achieving enlarging the vessel lumen, covering dissections and reducing restenosis rates in comparison to balloon angioplasty<sup>(4)</sup>.

The increased risk of restenosis after PCI in diabetic patients, including a higher rate of occlusive restenosis, translates into increased rates of target lesions- related ischemic events. In diabetic patients undergoing PTCA, restenosis manifesting as total vessel occlusion occurred in 13% of treated lesions and was associated with a reduction in left ventricular ejection fraction at six month follow up<sup>(5)</sup>.



In-stent restenosis has been applied to describe the development of significant luminal narrowing more than 50% at the site of the prior coronary intervention (angiographic restenosis), recurrence of symptoms and signs of ischemia after an initially successful revascularization (clinical restenosis) and to describe local neointimal hyperplasia at the site of catheter treatment (histological restenosis)<sup>(3)</sup>.

## Aim of the Work

### **This study was designed aiming at:**

- Studying the immediate procedural and in hospital outcome of PCI done to multivessel coronary artery disease.
- Identifying the short-term outcome and intermediate-term outcome of such procedure in diabetic and non diabetic patients.
- Comparing the short and intermediate-term outcome of PCI in diabetic versus non diabetic patients.
- Trying to detect the predictors of MACE in both groups after multivessel stenting.

## **Chapter (1)**

# Diabetes and Cardiovascular Disease

### Introduction:

This statement examines the cardiovascular complications of diabetes mellitus and considers opportunities for their prevention. These complications include coronary heart disease (CHD), stroke, peripheral arterial disease, nephropathy, retinopathy, and possibly neuropathy and cardiomyopathy. Because of the aging of the population and an increasing prevalence of obesity and sedentary life habits, the prevalence of diabetes is increasing. Thus, diabetes must take its place alongside the other major risk factors as important causes of cardiovascular disease (CVD). In fact, from the point of view of cardiovascular medicine, it may be appropriate to say, "Diabetes is a cardiovascular disease."

### Clinical presentation of Diabetes Mellitus:

The most prevalent form of diabetes mellitus is type 2 diabetes. This disorder typically makes its appearance later in life. The underlying metabolic causes of type 2 diabetes are the combination of impairment in insulin-mediated glucose disposal (insulin resistance) and defective secretion of insulin by pancreatic  $\beta$ -cells. Insulin resistance develops from obesity and

physical inactivity, acting on a substrate of genetic susceptibility<sup>[6]</sup>. Insulin secretion declines with advancing age,<sup>[7]</sup> and this decline may be accelerated by genetic factors<sup>[8]</sup>. Insulin resistance typically precedes the onset of type 2 diabetes and is commonly accompanied by other cardiovascular risk factors: dyslipidemia, hypertension, and prothrombotic factors<sup>[9]</sup>. The common clustering of these risk factors in a single individual has been called the metabolic syndrome. Many patients with the metabolic syndrome manifest impaired fasting glucose (IFG)<sup>[10]</sup>, even when they do not have overt diabetes mellitus<sup>[11]</sup>. The metabolic syndrome commonly precedes the development of type 2 diabetes by many years<sup>[12]</sup>; of great importance, the risk factors that constitute this syndrome contribute independently to CVD risk.

Recently, new criteria have been accepted for the diagnosis of diabetes<sup>[10]</sup>. The upper threshold of fasting plasma glucose for the diagnosis of diabetes has been lowered from  $\geq 140$  mg/dL to  $\geq 126$  mg/dL. The upper threshold for normoglycemia likewise has been reduced from  $< 115$  to  $< 110$  mg/dL. A fasting plasma glucose of 110 to 125 mg/dL is now designated IGF. These changes removed the need for oral glucose tolerance testing for diagnosis of diabetes; a diagnosis rests entirely on confirmed elevations of fasting plasma glucose. Furthermore, the terms insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus have been replaced by type 1 diabetes and type 2 diabetes, respectively<sup>[10]</sup>.

The other form of diabetes mellitus is type 1 diabetes, which follows immunologic destruction of pancreatic  $\beta$ -cells<sup>[13]</sup>. Type 1 diabetes usually begins early in life and is often called juvenile diabetes. This form of diabetes frequently produces microvascular complications, nephropathy, and retinopathy<sup>[13]</sup>, but it also predisposes to CHD<sup>[14]</sup>. Because type 2 diabetes occurs much more commonly than type 1 diabetes, the present statement will emphasize type 2 diabetes. Nonetheless, type 1 diabetes will be integrated into the overall strategy of cardiovascular risk reduction.

#### Diabetes as a major risk factor:

A large body of epidemiological and pathological data documents that diabetes is an independent risk factor for CVD in both men and women<sup>[15]</sup>. Women with diabetes seem to lose most of their inherent protection against developing CVD<sup>[15]</sup>, CVDs are listed as the cause of death in  $\approx 65\%$  of persons with diabetes<sup>[16]</sup>. Diabetes acts as an independent risk factor for several forms of CVD. To make matters worse, when patients with diabetes develop clinical CVD, they sustain a worse prognosis for survival than do CVD patients without diabetes<sup>[17]</sup>. These considerations have convinced the Scientific Advisory and Coordinating Committee of the American Heart Association (AHA) that diabetes mellitus deserves to be designated a major risk factor for CVD. This formal designation commits the AHA to a greater emphasis on diabetes as a risk factor in its scientific and educational programs. This statement

provides the scientific rationale for the decision to classify diabetes as a major risk factor for CVD.

### Atherosclerotic CHD:

Both type 1 diabetes and type 2 diabetes are independent risk factors for CHD<sup>[15]</sup>. Moreover, myocardial ischemia due to coronary atherosclerosis commonly occurs without symptoms in patients with diabetes<sup>[17]</sup>. As a result, multivessel atherosclerosis often is present before ischemic symptoms occur and before treatment is instituted. A delayed recognition of various forms of CHD undoubtedly worsens the prognosis for survival for many diabetic patients<sup>[15]</sup>.

### Diabetic Cardiomyopathy:

One reason for the poor prognosis in patients with both diabetes and ischemic heart disease seems to be an enhanced myocardial dysfunction leading to accelerated heart failure (diabetic cardiomyopathy)<sup>[18]</sup>. Thus, patients with diabetes are unusually prone to congestive heart failure. Several factors probably underlie diabetic cardiomyopathy: severe coronary atherosclerosis, prolonged hypertension, chronic hyperglycemia, microvascular disease, glycosylation of myocardial proteins, and autonomic neuropathy. Improved glycemic control, better control of hypertension, and prevention of atherosclerosis with cholesterol-lowering therapy may prevent or mitigate diabetic cardiomyopathy. An early clinical trial<sup>[19]</sup>, suggested that sulfonylureas used for control of

hyperglycemia are cardiotoxic and may exacerbate diabetic cardiomyopathy. This side effect, however, was not confirmed in a recent large clinical trial<sup>[20]</sup>.

### Stroke:

Mortality from stroke is increased almost 3-fold when patients with diabetes are matched to those without diabetes<sup>[21]</sup>. The most common site of cerebrovascular disease in patients with diabetes is occlusion of small paramedial penetrating arteries<sup>[22]</sup>. Diabetes also increases the likelihood of severe carotid atherosclerosis. Patients with diabetes, moreover, are likely to suffer irreversible brain damage with carotid emboli that otherwise would produce only transient ischemic attacks in persons without diabetes. Approximately 13% of patients with diabetes >65 years old have had a stroke<sup>[23-24]</sup>.

### Renal Disease:

Renal disease is a common and often severe complication of diabetes<sup>[25]</sup>. Approximately 35% of patients with type 1 diabetes of 18 years' duration will have signs of diabetic renal involvement<sup>[26]</sup>. Up to 35% of new patients beginning dialysis therapy have type 2 diabetes<sup>[27]</sup>. End-stage renal disease (ESRD) appears to be especially common among Hispanics, blacks, and Native Americans with diabetes<sup>[28]</sup>. For patients with diabetes who are on renal dialysis, mortality rates probably exceed 20% per year<sup>[22]</sup>. When diabetes is present, CVD is the leading cause of death among patients with ESRD<sup>[29]</sup>.