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شبكة المعلومات الجامعية

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التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

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

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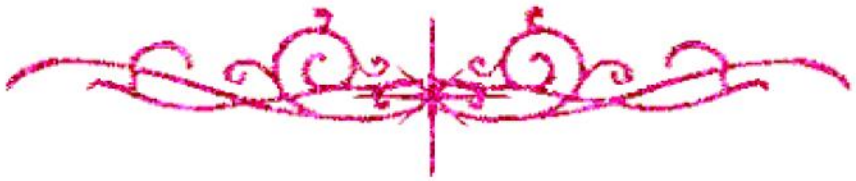
بعض الوثائق الأصلية تالفة



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بالرسالة صفحات

لم ترد بالأصل

HOSSAM MAGHRABY

Latent cardiac abnormalities in patients with recently diagnosed type 2 diabetes mellitus

Thesis submitted in partial fulfillment for the MD degree in cardiology

BY

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Dedication

To my parents and my family:
A sincere work dedicated to sincere people

Acknowledgment

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Ramadan Ghaleb.

Contents

Abbreviations

ACE:	Angiotensin converting enzyme
ADA:	American Diabetes Association
ADP:	Adenosine diphosphate
AGEs:	Advanced glucose end-products
ALFEDIAM:	Association de Langue Francaise pour Etude du Diabetes Maladies Metaboliques
ATP:	Adenosine triphosphate
BMI:	Body mass index
BNP:	Brain natriuretic peptide
CHD:	Coronary heart disease
CRP:	C-reactive protein
CVD:	Cardiovascular disease
DKA:	Diabetic Ketoacidosis
ERDS:	End stage renal disease
ET-1:	Endothelin-1
FADH2:	Flavin adenine dinuclotide
FBG:	Fasting blood glucose
FDG:	Fluoro deoxyglucose
FFA:	Free fatty acid
GAD:	Glutamic acid decaboxylase
GDM:	Gestational diabetes mellitus
GFR:	Glomerular Filtration rate
GLUT:	Glucose transporters family
GPs:	Glycoproteins
HDL:	High density lipoprotein
HHNS:	Hyperosmolar hyperglycemia non ketotic syndrome
HLA:	Human leuckocyte antigen
HOPE:	Heart Outcome Prevention Evaluation study
HSPG:	Heparin Sulphate proteglycen
IAA:	Insulin Autoantibodies
ICA:	Islet cell antibody
ICAM:	Intracellular adhesion molecules
IDDM:	Insulin dependent diabetes mellitus
IGT:	Impaired glucose tolerance
IVRT:	Isovolumetric relaxation time
LDL:	Low density lipoprotein
LVDD:	Left ventricular diastolic dysfunction
LVH:	Left ventricular hypertrophy
LVMI:	Left ventricular mass index
M-CSF:	Macrophages colony stimulating factor
MI:	Myocardial infarction
MODY:	Maturity onset diabetes of the young
NADH:	Nicotinamide adenine dinuclotide
NIDDM:	Non Insulin dependent diabetes mellitus
NOSIII:	Nitric oxide synthesis III
OGIT:	Oral glucose impaired tolerance

PAI-1:	Plasminogen activator inhibitor-1
PAS:	Para aminosylcylic acid
PAS:	Periodic Acid Schiff
PDH:	Pyurvate dehydrogenase
PECAM:	Platelet endothelial cell adhesion molecule
PKC:	Protein kinase C
POCS:	Polycystic ovarian syndrome
RAGEs:	Receptor of advanced glucose end-products
SMI:	Silent myocardial ischemia
TG:	Triglyceride
TMS:	Thallium myocardial scintigraphy
TNF;	Tissue necrosis factor
UKPDS:	United Kingdom prospective study
VCAM:	Vascular cell adhesion molecule
VCMCs:	Vascular smooth muscle cells
VLDL:	Very low density lipoprotein
WHO:	World health organization

Introduction and Aim of the Work

Introduction

Diabetes mellitus is an important independent risk factor for atherosclerotic related disease. Specifically diabetic patients carry a three fold increased risk of developing cardiac abnormalities in the form of ischaemic heart disease, left ventricular hypertrophy, diabetic cardiomyopathy and/or autonomic dysfunction. When diabetes and ischaemic heart disease coexist the later is usually more severe and consequently prognosis is worse **(Hanefold et al., 1997).**

Increased cardiovascular mortality occurs in diabetic patients with or without coronary heart disease. This is attributed to the presence of diabetic cardiomyopathy, the potential mechanism of which is hyperglycemia that has been reported to activate protein kinase C (PKC), which has been associated with the development of microvascular and macrovascular pathology in diabetes mellitus **(Way, 2002).**

Recent studies suggest that left ventricular hypertrophy is very frequent in diabetic patients **(Sachs et al.,1999)** and that it might be of genetic basis such as mitochondrial Deoxy ribonucleic acid (DNA) abnormalities **(Momiyoma et al.,1999)** Biochemical abnormalities such as a decrease in the Active form of pyruvate dehydrogenase were reported in diabetic patients with left ventricular hypertrophy which results in impairment of myocardial substrate delivery to the mitochondria that may finally lead to energy depleted state observed in heart failure **(Seymour et al., 1997)**

Prolonged QT dispersion has been shown in several studies to be a strong and independent predictor of cardiac abnormalities and cardiac death in type2 diabetes mellitus **(Bushras et al.,2002).**

Cardiovascular complications in patients with type 2 diabetes are likely to have had their genesis long before the diagnosis of this disease. In the United Kingdom Prospective Diabetes Study (UKPDS), ~20% to 25% of newly diagnosed patients with type 2 diabetes had evidence of atherosclerosis **(Nathan, 2002)**. In type 2 diabetes, there is no obvious association between the extent or severity of macrovascular complications and the duration or severity of the disease. An increased prevalence of coronary artery disease is apparent in newly diagnosed type 2 diabetes subjects. This finding may reflect an important element of insulin resistance in the pathogenesis of this condition. Such resistance begins one or more decades before diagnosis, and may be associated with a multifactorial, high-risk cardiovascular state known as the metabolic syndrome **(Uusitupa et al., 1985).**

It is well known that diabetes is associated with other risk factors for heart disease, such as older age, abdominal obesity, hypertension and dyslipidaemia. It is clear that diabetes is an independent risk factor for heart disease even after controlling other traditional risk factors **(Haffiner et al., 1998).**

There is growing evidence that one of the most important emerging risk factors is hyperglycemia. By definition, people with diabetes are hyperglycemic at the time of diagnosis. Moreover, there is usually a five to seven year period of undiagnosed diabetes preceding the diagnosis of diabetes **(Laakso M.1999).**

Hyperglycemia is developed gradually, and at earlier stages it is often not severe enough for the patient to notice any classic symptoms of diabetes mellitus. Such patients are at increased risk of developing macrovascular and microvascular complications **(Stratton et al; 2000).**

Hyperglycemia appears to be the determinant of microvascular and metabolic complications. However, glycemia is much less related to macrovascular disease. Cardiovascular risk is determined by many factors including: Insulin resistance with concomitant lipid levels (small, dense, low-density lipoprotein [LDL] particles; low high-density lipoprotein-cholesterol (HDL-C), and elevated remnant lipoproteins and thrombotic abnormalities (elevated type-1 plasminogen activator inhibitor [PAI-1] and elevated fibrinogen), as well as conventional atherosclerotic risk factors (family history, smoking, hypertension, elevated low-density lipoprotein-cholesterol [LDL-C], and low HDL-C). Increased cardiovascular risk appears to begin prior to the development of frank hyperglycemia, presumably due the effects of insulin resistance. Stern and Haifner have developed the ticking clock hypothesis of complications, asserting that the clock starts ticking for microvascular risk at the onset of hyperglycemia, while the clock starts ticking for macrovascular risk at some antecedent point, presumably with the onset of insulin resistance. **(William et al., 2004)**

However, last decade mortality from cardiovascular disease has shown an annual decline which may be largely due to improvement in the treatment and secondary prevention of myocardial infarction and congestive heart failure: a progressive disease that has emerged as one of the leading cardiovascular disorders in developed countries and is expected to become a major disease burden by the year 2020 **(Feuerstin et al., 1997).** This situation emphasizes the necessity of risk reduction among asymptomatic subjects in order to prevent clinical symptoms of cardiovascular disease i.e. primary prevention **(Orchard et al., 1998).**