

TISSUE DOPPLER IMAGING IDENTIFIES NORMOTENSIVE DIABETIC PATIENTS WITH CARDIOMYOPATHY

Thesis

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LIST OF ABBREVIATIONS

A	Peak atrial contraction velocity.
AGE	Advanced glycation end product
E	Peak early transmitral flow velocity.
IVC	Inferior vena cava.
BNP	B-type natriuretic peptide
LA	Left atrium.
RAS	Renin angiotensin system
LV	Left ventricle or ventricular.
LV-EDP	Left ventricular end-diastolic pressure.
LV-EDV	Left ventricular end-diastolic volume.
LV-EF	Left ventricular ejection fraction.
LV-ESP	Left ventricular end-systolic pressure.
LV-ESV	Left ventricular end-systolic volume.
tau	Time constant of isovolumic relaxation.
TD	Time delay.
TEE	Trans-oesophageal echocardiography.
v_p	Color M-mode flow propagation velocity.
SBP	Systolic Blood Pressure.
DBP	Diastolic Blood Pressure.
ECG	Electrocardiogram.
DM	Diabetes mellitus.
FBG	Fasting Blood Glucose.
WHO	World Health Organization
IFG	Impaired Fasting Glucose.
IDDM	Insulin-Dependent Diabetes Mellitus.
NIDDM	Non-Insulin Dependent Diabetes Mellitus.
OGTT	Oral Glucose Tolerance Test.
IGT	Impaired Glucose Tolerance.
GDM	Gestational Diabetes Mellitus.

β -CELL	Beta Cell.
ICAs	Islet Cell Autoantibodies.
IAAs	Insulin Autoantibodies.
GLUT	Glucose uptake
GADAs	Glutamic acid Decarboxylase Autoantibodies.
DKA	Diabetic Ketoacidosis.
CVD	Cardiovascular Disease.
AHA	American Heart Association.
CHD	Coronary Heart Disease.
MI	Myocardial Infarction.
FHS	Framingham Heart Study.
UKPDS	United Kingdom Prospective Diabetes Study.
HF	Heart Failure.
TDI	Tissue Doppler Imaging.
MVG	Myocardial velocity Gradient.
ETDI	Early Filling Phase.
ATDI	Late Filling Phase.
ACE.	Angiotensin Converting Enzyme.
E/E'	Peak Early Diastolic Flow Velocity to Peak Ring Velocity.
IVRT.	Isovolumetric Relaxation Time.

INTRODUCTION AND AIM OF WORK

INTRODUCTION

Diabetes mellitus is a state of chronic hyperglycemia and can be defined as a state of diminished insulin action due to its decrease availability or effectiveness in varying combination **(Bell and Hockady, 2001)**. In addition, diabetes can defined as a disease that affects the body's ability to produce or respond to insulin, a hormone that allows blood glucose to enter to the cells of the body & be used for energy. **(American Heart Association, 2003)**.It is associated with late complications involving eyes, kidneys, heart, nerves & blood vessels. **(American heart assosiation,2009)**.

The most life-threatening consequences of diabetes are heart disease and stroke, which strike people with diabetes more than twice as often as they do others. Most of the cardiovascular complications related to diabetes have to do with the way the heart pumps blood through the body. Diabetes can change the chemical makeup of some substances found in the blood and this can cause blood vessels to develop early onset atherosclerosis. More than 65% of deaths in

diabetic population are attributed to heart & vascular disease (*American Heart Association, 2003*).

In most cardiac conditions that affect the myocardium, an impairment of active relaxation is frequently the first abnormality to occur. Therefore, early detection and evaluation of the severity of this impairment could lead to an earlier application of preventive measures to delay or avoid the occurrence of clinical heart failure. (*American heart association, 2009*)

Left ventricular diastolic dysfunction represent the earliest preclinical manifestation of diabetic cardiomyopathy that can progress to symptomatic heart failure. Recent studies have demonstrated up to 60% of asymptomatic normotensive patients with diabetes mellitus have diastolic dysfunction when assessed by conventional echocardiography including the response to Valsalva maneuver. (*Poirier et al., 2001*)

Using recent echocardiographic techniques such as tissue Doppler imaging (TDI) have significantly improved the ability to accurate detection of diastolic dysfunction (*John et al., 2004*).

In contrast to conventional echocardiography, TDI directly derives velocity information from within the myocardial wall without need for endocardial boundary

AIM OF THE WORK

Studying the efficacy of tissue Doppler imaging to identify diastolic dysfunction, this is the earliest sign of diabetic cardiomyopathy in asymptomatic normotensive diabetic patients.

CHAPTER

(1)

DIABETES MELIITUS

Definition of Diabetes Mellitus:

Diabetes mellitus is a group metabolic disease characterized by chronic hyperglycemia and disturbance of carbohydrates, lipids and proteins metabolism with disturbance of water and electrolytes homeostasis resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eye, kidney, heart and blood vessels (*Alberti and Zimmet, 1998*).

Disturbed glucose metabolism and its sequelae are becoming the most common contributors to the development of cardiovascular disease. Indeed, the relative importance of “diabesity” as a risk factor is greater than ever, reflecting the epidemic of obesity on the one hand and better Control of many risk factors, such as smoking and hypercholesterolemia, on the other. However, these adverse cardiovascular effects relate predominantly to the development of atherosclerosis, 1 but in parallel with this (and no less malignant) are the effects of diabetes and abnormal glucose metabolism on myocardial function. The most common initial manifestation of this is diastolic dysfunction (*John et al., 2003*).

Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome (*The Expert Committee on The diagnosis of DM, 2003*).

Hyperglycemia was defined as random plasma glucose concentration of the venous sample greater than 200 mg/dL (*Alberti and Zimmet, 1998*).

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the β -cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action frequently Coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause

of the hyperglycemia (*The American diabetes association, 2002*).

Prevalence of diabetes mellitus:

Diabetes mellitus is one of chronic diseases with world wide distribution. DM affects an estimated 6% of the population of the United States, about half of whom are undiagnosed. Incidence is greater in females and rises with age. Type 2 accounts for 90% of cases. (*The expert committee on the diagnosis of DM, 2002*).

The American Diabetes Association reported in 2009 that there are 23.6 million children and adults in the United State — 7.8% of the population, who have diabetes. While an estimated 17.9 million in the US alone have been diagnosed with diabetes, nearly one in four (5.7 million) diabetics are unaware that they have the disease. (*American Diabetes assosiation,2009*).

The new diagnostic criteria for diabetes recommended by the American Diabetes Association in 1997 will increase the prevalence of diabetes from 7.2% to 7.7% in European populations.

In elderly groups with a high prevalence of diabetes the increase in prevalence would be substantially higher.

Among 17 881 men and 8309 women, 1517 were classified as having diabetes according to either the American or WHO criteria.

Among these 1517 only 28% were classified as having diabetes according to criteria of both organizations (***Alberti and Zimmet, 1998***)

Type II diabetes mellitus is the predominant form of diabetes worldwide accounting for 90% of cases globally (***John et al., 2003***).

Diabetes is the third leading cause of death in the United States after heart disease and cancer (***The American diabetes association, 2003***).

Pathophysiology

Mechanism of insulin release in normal pancreatic beta cells, Insulin production is more or less constant within the beta cells, irrespective of blood glucose levels. It is stored within vacuoles pending release, via exocytosis, which is primarily triggered by food, chiefly food containing absorbable