



**Right Ventricular Function Assessment in
patients with chronic stable angina with Type
II DM Versus Non Diabetic Patients by TAPSE
and TDI Echocardiography**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Contents

Title	Page No.
List of Tables	
List of Figures	
List of Abbreviations	
Introduction	1
Aim of the Study	2
Review of Literature	—
Cardiovascular Complications of Diabetes Mellitus	3
RV functional assessment	26
Patients and Methods	46
Results	52
Discussion	67
Conclusion	73
Study limitations	74
Recommendations	75
Summary	76
References	80
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Shows the basic characteristics of all the candidates.	52
Table (2):	Shows the anatomy and significance of coronary lesions	55
Table (3):	Echocardiographic data	56
Table (4):	Shows the comparison between both groups regarding age and sex.	59
Table (5):	Shows the comparison between both groups regarding the risk factors.	60
Table (6):	Shows the comparison between both groups regarding the anatomy and significance of CA findings.	62
Table (7):	Shows the comparison between both groups regarding Echocardiographic data	63

List of Figures

Fig. No.	Title	Page No.
Figure (1):	The “common soil” hypothesis of diabetes complications. ROS, reactive oxygen species ⁽⁵²⁾	13
Figure (2):	Coagulation and platelet reactivity in diabetes. In patients with diabetes chronic hyperglycemia and insulin resistance determine a significant alteration in the coagulation factors as well as increased platelet aggregation, leading to a prothrombotic state.	15
Figure (3):	Mechanisms of diabetic cardiomyopathy. ⁽⁶⁰⁾	20
Figure (4):	Coronary artery system ⁽⁷⁶⁾	27
Figure (5): RCA course & branches ⁽⁷⁷⁾		28
Figure (6): RCA branches & segments supplied by it ⁽⁷⁶⁾		28
Figure (7):	Diagram showing the recommended apical 4-chamber (A4C) view with focus on the right ventricle (RV) (1*) and the sensitivity of right ventricular size with angular change (2,3) despite similar size and appearance of the left ventricle (LV). The lines of intersection of the A4C planes (1*,2,3) with a mid left ventricular short-axis are shown above and corresponding A4C views below ⁽³⁾	36
Figure (8):	Diagram (left) and corresponding echocardiographic apical 4-chamber image (right) showing the right ventricular (RV) basal (RVD1) and mid cavity (RVD2) RV minor dimensions and the RV longitudinal dimension (RVD3). The transducer is adjusted to focus on the RV chamber, with the goal of maximizing RV chamber size. The RV free wall is better seen in this view, also facilitating measurements for fractional area change. ⁽⁹⁵⁾	37
Figure (9):	Measurement of tricuspid annular plane systolic excursion (TAPSE) ⁽⁹⁴⁾	38

List of Figures

Fig. No.	Title	Page No.
Figure (10):	Examples of right ventricular fractional area change (FAC). The endocardial border is traced in apical 4-chamber (A4C) views from the tricuspid annulus along the free wall to the apex, then back to the annulus, along the interventricular septum at end-diastole (ED) and end-systole (ES). (Left) Normal subject, FAC 60%. (Middle) Moderately dilated right ventricle (RV), FAC 40%, and a markedly dilated left ventricle (LV). (Right) Dilated RV, FAC 20%, and the LV is foreshortened as a result of optimizing the view for the right ventricular chamber ⁽³⁾	40
Figure (11):	Tissue Doppler of the tricuspid annulus in a patient with normal right ventricular systolic function ⁽³⁾	41
Figure (12):	Measurement of tricuspid annular plane systolic excursion (TAPSE) in patient number 30.....	51
Figure (13):	Tissue Doppler of the tricuspid annulus in a patient number 11 with normal RV systolic function s' '17cm/s'.	51
Figure (14):	Shows the gender distribution among the patients.....	53
Figure (15):	Shows the smoking status among the patients.	54
Figure (16):	Shows the HTN distribution among the patients.	54
Figure (17):	Shows the anatomy of RCA lesions among the patients.	55
Figure (18):	Shows the significance of LAD lesions among the patients.	56
Figure (19):	Shows the distribution of SWMA among the patients.	57
Figure (20):	Shows the MV state among the patients.	58
Figure (21):	Shows the TV state among the patients.	58
Figure (22):	Shows the comparison of age in both groups.....	59
Figure (23):	Shows the comparison of sex in both groups.....	60
Figure (24):	Shows the comparison of smoking in both groups.	61
Figure (25):	Shows the comparison of HTN in both groups.....	61

List of Figures

Fig. No.	Title	Page No.
Figure (26):	Shows the comparison of significance of LAD lesions in both groups.	62
Figure (27):	Shows the comparison of EF in both groups.	64
Figure (28):	Shows the comparison of SWMA in both groups.....	64
Figure (29):	Shows the comparison of MV state in both groups	65
Figure (30):	Shows the comparison of TV state in both groups.	65
Figure (31):	Shows the comparison of TAPSE in both groups.....	66
Figure (32):	Shows the comparison of S' in both groups.....	66

List of Abbreviations

Abb.	Full term
	Cardiovascular disease (CVD)
	tricuspid annular plane systolic excursion (TAPSE),
	DTI-derived tricuspid lateral annular systolic velocity wave (S'),
	fractional area change (FAC),
	RV index of myocardial performance (RIMP).
	peripheral vascular disease (PVD)
	coronary artery disease (CAD).
	American Heart Association (AHA)
	Low density lipoprotein 'LDL'
	high density lipoprotein' HDL
	nitric oxide (NO)
	Diabetic autonomic neuropathy (DAN)
	reactive oxygen species (ROS)
	myocardial infarction 'MI'
	plasminogen activator inhibitor PAI
	TF:tissue factor
	t-PA :tissue plasminogen activator
	VWF:Von Welbrand factor
	peak systolic velocity (Sm), peak early diastolic velocity (Em), peak late diastolic velocity (Am)

INTRODUCTION

Cardiovascular disease (CVD) is one of the most common comorbidities and causes of death in patients with diabetes mellitus ⁽¹⁾.

Diabetic cardiomyopathy refers to myocardial dysfunction independent of coronary artery disease. The underlying mechanisms are proposed to be multifactorial, including microangiopathy and myocardial fibrosis ⁽²⁾.

Echocardiographic assessment of the right side of the heart is gaining importance in current clinical practice and research with guidelines recently published specifically to address this purpose ⁽³⁾. This is because of growing evidence of its effects on clinical outcome, morbidity and mortality of several cardiac conditions ^(4,5)

Accurate evaluation of the systolic function of the RV is better achieved by measuring one or many echocardiographic indices, and an integrative approach using a combination of parameters is preferred. These parameters comprise the tricuspid annular plane systolic excursion (TAPSE), DTI-derived tricuspid lateral annular systolic velocity wave (S'), fractional length shortening, fractional area change (FAC) and RV index of myocardial performance (RIMP). (3,6).

AIM OF THE STUDY

The aim of this study is to assess RV function by TAPSE and TDI echocardiography in patients with significant RCA lesions in Type II DM versus non diabetic patients.

Chapter 1

CARDIOVASCULAR COMPLICATIONS OF DIABETES MELLITUS

Diabetes mellitus is a prime risk factor for cardiovascular disease (CVD). Vascular disorders include retinopathy and nephropathy, peripheral vascular disease (PVD), stroke, and coronary artery disease (CAD). Diabetes also affects the heart muscle, causing both systolic and diastolic heart failure. Evidence suggests that although hyperglycemia, the hallmark of diabetes, contributes to myocardial damage after ischemic events, it is clearly not the only factor, because both pre-diabetes and the presence of the metabolic syndrome, even in normoglycemic patients, increase the risk of most types of CVD.⁽⁷⁻¹⁰⁾

A large body of epidemiological and pathological data documents that diabetes is an independent risk factor for CVD in both men and women. Women with diabetes seem to lose most of their inherent protection against developing CVD. CVD is listed as the cause of death in approximately 65% of patients with diabetes. To make matters worse, when patients with diabetes develop clinical CVD, they sustain a worse prognosis for survival than do CVD patients without diabetes. 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. ⁽¹¹⁻¹²⁾

Type 2 diabetes, the most common form of the disease, may remain undetected for many years and its diagnosis is often made incidentally through an abnormal blood or urine glucose test. Hence, physicians often face this disease at an advanced stage when vascular complications have already occurred in most of the patients. Macrovascular complications are mainly represented by atherosclerotic disease and its sequelae. Diabetes-related microvascular disease such as retinopathy and nephropathy are major causes of blindness and renal insufficiency. ⁽¹³⁾

Based on this scenario, a better understanding of the mechanisms underlying diabetic vascular disease is mandatory because it may provide novel approaches to prevent or delay the development of its complications.

Pathophysiology of diabetes mellitus-related cardiovascular complications:

The pathophysiology of the link between diabetes and cardiovascular disease (CVD) is complex and multifactorial. Understanding these profound mechanisms of disease can help clinicians identify and treat CVD in patients with diabetes, as well as help patients prevent these potentially devastating complications. ⁽⁷⁾

A- Macrovascular Disease:

Atherosclerosis is the major threat to the macrovasculature for patients with and without diabetes.¹ But several factors specific to diabetes are worth mentioning. Clinically, dyslipidemia is highly correlated with atherosclerosis, and up to 97% of patients with diabetes are dyslipidemic.⁽¹⁵⁾ In addition to the characteristic pattern of increased triglycerides and decreased HDL cholesterol found in the plasma of patients with diabetes, abnormalities are seen in the structure of the lipoprotein particles. In diabetes, the predominant form of low density lipoprotein 'LDL' cholesterol is the small, dense form. Small LDL particles are more atherogenic than large LDL particles because they can more easily penetrate and form stronger attachments to the arterial wall, and they are more susceptible to oxidation. Because less cholesterol is carried in the core of small LDL particles than in the core of large particles, subjects with predominantly small LDL particles have higher numbers of particles at comparable LDL cholesterol levels.⁽¹⁶⁾

Oxidized LDL is pro-atherogenic because once the particles become oxidized they acquire new properties that are recognized by the immune system as "foreign." Thus, oxidized LDL produces several abnormal biological responses, such as attracting leukocytes to the intima of the vessel, improving the ability of the leukocytes to ingest lipids and differentiate into

foam cells, and stimulating the proliferation of leukocytes, endothelial cells, and smooth muscle cells.⁽¹⁷⁾

All of which are steps in the formation of atherosclerotic plaque. In patients with diabetes, LDL particles can also become glycated, in a process similar to the glycation of the protein hemoglobin (measured in the hemoglobin A_{1c} [A1C] assay). Glycation of LDL lengthens its half-life⁽¹⁸⁾ and therefore increases the ability of the LDL to promote atherogenesis. Paradoxically, however, glycation of ‘high density lipoprotein’ HDL shortens its half-life and renders it less protective against atherosclerosis.⁽¹⁹⁾

Moreover, diabetic blood is more likely to be high in triglycerides. Hypertriglyceridemia in diabetes occurs, in part, because insulin action regulates lipid flux. Insulin promotes the activity of the enzyme lipoprotein lipase, which mediates free fatty acid uptake into adipose tissue (storage) and also suppresses the activity of the enzyme hormone-sensitive lipase, resulting in decreased release of free fatty acids into the circulation.⁽²⁰⁾ Hypertriglyceridemia can lead to increased production of the small, dense form of LDL and to decreased HDL transport of cholesterol back to the liver.⁽²¹⁾

Dyslipidemia is only one mechanism by which diabetes promotes atherosclerosis; endothelial dysfunction often contributes. Healthy endothelium regulates blood vessel tone, platelet activation, leukocyte adhesion, thrombogenesis, and