## Gender Differences of Pulsed and Tissue Doppler Indices of Left Ventricular Diastolic Function in Type II Diabetic Patients

## Thesis

Submitted for partial fulfillment of the master degree in **Cardiology** 

### **B**γ **Hani Ibrahim Elalam**

(M.B.B.CH) Benghazi University

Under Supervision of

## **Prof.Dr. Walid Abdel Azim El-Hammady**

Professor of Cardiology
Faculty of Medicine - Ain Shams University

## Dr. Mohamed Helmy Mohamed Radwan

Lecturer of Cardiology Faculty of Medicine – Ain Shams University

Faculty of Medicine Ain-Shams University **2016** 



# بسم الله الرحمن الرحيم

"رَبِّ أُونْ ِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ اللَّتِي أَنْعَمْتَ عَلَيَّ وَرَانِ أَشْكُرَ نِعْمَتَكَ اللَّتِي أَنْعَمْتَ عَلَيَّ وَكَانِي وَكَانِي وَرَانِ أَعْمَلَ صَالِعًا تَرْضَاهُ وَلَانُ خِلْنِي وَعَلَى وَالْمِرِيُّ وَلَنْ لَعْمَلَ صَالِعًا تَرْضَاهُ وَلَامْ لِنِي اللَّهِ اللَّهِ اللَّهِ اللَّهِ اللَّهُ المَّالِحِينَ " برَحْمَتِكَ فِي عِبَاوكَ (الصَّالِحِينَ "

## صدق الله العظيم

سورة النمل الآية (١٩)





First of all, I should express my deep thanks to **Allah**, without his great blessing, I would never accomplish my work, and to whom I relate any success in achieving any work in my life.

I would like to express my sincere appreciation and deepest gratitude to **Prof. Dr. Walid Abdel Azim ElHammady**, Professor of Cardiology, Faculty of Medicine - Ain Shams University; for his help in choosing the topic of this study, his meticulous advice, continuous encouragement and valuable instructions all through this work. It was a pleasure and privilege to work under his guidance and supervision.

I am deeply grateful to **Dr. Mohamed Helmy Mohamed Radwan**, Lecturer of Cardiology, Faculty of
Medicine - Ain Shams University, every word and every step in
this work has been kindly arranged by her sincere effort, care and
continuous encouragement.

Finally my truthful affection and love to My Family, who were and will always be, by my side all my life.

## **List of Contents**

Subject	Page No.
List of Abbreviations	
List of Tables	iii
List of Figures	v
Introduction	1
Aim of the Work	4
Review of Literature	
Effect of Diabetes on Diastolic Function	5
Role of Echocardiography in Assessment of Diastolic Function	
Patients and Methods	34
Results	42
Discussion	74
Summary	87
Conclusion	91
Limitations	92
Recommendations	93
References	94
Arabic Summary	—

#### **List of Abbreviations**

Abbr. Eitle

**ADA** : American diabetic association

Ar velocity : Atrial reversal velocityATP : Adenosine triphosphateCAD : Coronary artery disease

**CHARM PRESERVED** candesartan in heart failure preserved trial

CMR : Cardiac magnetic imaging
CVD : Cardiovascular disease
CWD : Continuous wave Doppler
DBP : Diastolic blood pressure
DD : Diastolic dysfunction
DHE : Diastolic heart feilura

DHF : Diastolic heart failureDHF : Diastolic heart failure

DM : Diabetes mellitusDT : Deceleration time

DTI : Tissue Doppler imageECG : ElectrocardiogramED : Diastolic elastance

**EDD** : End diastolic diameter

**ESC** : European society of cardiology

**ESD** : End systolic diameter

**ESH** : European society of hypertension

**HF** : Heart failure

**HFNEF** : Heart failure normal ejection fraction

**HR** : Heart rate

**BP** : Blood pressure

LAD : Left atrial dimension
HBA1c : glycosylated hemoglobin

#### List of Abbreviations

**ICTP** : Carboxy terminal telopeptide collagen

**IVRT** : Isovolumetric Relaxation Time

**LV** : Left Ventricular

**LVEDP** : Left ventricular end diastolic pressure

**LV** : Left ventricle

**LVEF** : Left ventricular ejection fraction

**MMPs** : Matrix metalloproteinase

**NIDDM** : Non insulin dependence diabetes mellitus

**PIIINP** : Serum aminoterminal peptide

**PNF** : Pseudonormal left ventricular filling

**PVAT** : Perivascular Adipose Tissue

**PWD** : Pulsed wave Doppler

**RAAS** : Renin angiotensin aldosterone system

ROS : Reactive Oxygen Species
SBP : Systolic blood pressure

**SD** : Standard deviation

**SERCA** : Sarcoplasmic reticulum–calcium ATPase

**SPSS** : Statistical package of special science

**SR** : Sarcoplasmic reticulum

**SV** : Stroke volume

**T2DM**: Type 2 diabetes mellitus

**TD** : Tissue Doppler

TTE : Transthoracic echocardiography

TVI : Tissue velocity image VP : Propagation velocity

**WHO** : World health organization

## **List of Tables**

Cable No	v. Eitle	Page No.
<b>Table (1):</b>	Demographic data of the study group	os 42
<b>Table (2):</b>	Echocardiographic data of the study	group 44
<b>Table (3):</b>	Comparison between study and group as regard all the demographic	
<b>Table (4):</b>	Comparison between study and group as regard all Echocardio parameters	graphic
<b>Table (5):</b>	Comparison between Diabetic Ma Diabetic Female as regard all demographic data	of the
<b>Table</b> (6):	Comparison between diabetic madiabetic female as regard echocardiographic parameters	all
<b>Table (7):</b>	Comparison between Non Diabetic and Non Diabetic Female as regard the study groups	d all of
<b>Table (8):</b>	Comparison between Non Diabetic M Non Diabetic Female as rega Echocardiographic parameters	rd all
<b>Table (9):</b>	Comparison between Diabetic Ma Non Diabetic Male as regard all study groups	of the
<b>Table (10):</b>	Comparison between Diabetic Ma Non Diabetic male as regar Echocardiographic parameters	ale and

#### List of Tables

<b>Table (11):</b>	Comparison between Diabetic Female and Non Diabetic Female as regard all of the study groups
<b>Table (12):</b>	Comparison between Diabetic Female and
	Non Diabetic Female as regard all
	Echocardiographic parameters65

## **List of Figures**

Figure No.	Citle	Page No.
Figure (1):	(A) Left Ventricular Arch Arrangement of fibers in a double fiber orientation changes from the the subepicardium to the right subendocardium (B)The arrows re the components that result from the developed in each fiber subendocardium and subepicardium	e helix - e left in in the epresent he force of the
Figure (2):	Color M-mode Vp from a patied depressed EF and impaired LV relationships and the color of the co	
Figure (3):	Mitral inflow, septal and lateral Doppler signals from a 60-year-old with heart failure and normal EF	d patient
Figure (4):	Measurement of left ventricular diastolic diameter and endediameter from M-mode, guid parasternal short-axis image	-systolic led by
Figure (5):	Illustration of Pulsed Wave-T Color-TDI with quantitative and the septal motion recorded in a patient	lysis of healthy
<b>Figure</b> (6):	Comparison between Study and group as regard Serum Creatinine	
<b>Figure (7):</b>	Comparison between Study and group as regard E/é lateral	
Figure (8):	Comparison between Study and group as regard E/é Septal	Control

Figure (9):	Comparison between Study and Control group as regard DT
<b>Figure (10):</b>	Comparison between Non Diabetic Male and Non Diabetic Female as regard Smoking Status
Figure (11):	Comparison between Non diabetic male and Non diabetic females as regard HR55
<b>Figure (12):</b>	Comparison between Non diabetic male and Non diabetic females as regard EF 57
<b>Figure (13):</b>	Comparison between Non diabetic male and Non diabetic females as regard LVEDD
<b>Figure</b> (14):	Comparison between Diabetic male and Non diabetic male as regard Creatinine 60
<b>Figure (15):</b>	Comparison between Diabetic male and Non diabetic male as regard E/é lateral 62
Figure (16):	Comparison between Diabetic male and Non diabetic male as regard E/é septal 63
<b>Figure</b> (17):	Comparison between Diabetic female and Non diabetic female as regard EF
<b>Figure (18):</b>	Comparison between Diabetic female and Non diabetic female as regard LA Diameter
<b>Figure (19):</b>	Comparison between Diabetic female and Non diabetic female as regard LVEDD 68
<b>Figure (20):</b>	Comparison between Diabetic female and Non diabetic female as regard DT 69
<b>Figure (21):</b>	36-year old non-diabetic male with normal diastolic function

#### List of Figures

<b>Figure (22):</b>	25-year old type II diabetic female patient with normal diastolic function	71
<b>Figure (23):</b>	20-year old non-diabetic female with normal diastolic function	72
Figure (24):	40-year old type II diabetic male patient assessed by tissue Doppler with grade II diastolic dysfuction	73

#### **Abstract**

**Background:** Diabetes mellitus characterized by hyperglycemia associated with disturbances of carbohydrate, protein and fat metabolism. With absolute or relative deficiencies in insulin secretion and/ or insulin action. The disease causes significant organ dysfunction with acute and long term complications that results in diabetes related morbidity and mortality. Aim of the Work: To assess gender differences of left ventricular diastolic function by pulsed and tissue Doppler echocardiographic indices in patients with type II diabetes mellitus. Patients sand Methods: This study was conducted in the Cardiology Department (Faculty of Medicine, Ain-Shams University), it was an observational case control study started from December 2015 to July 2016. Patients with type 2 DM were age and sex matched with healthy volunteers as control. The study included 100 patients (40 males and 60 females) with type II Diabetes Mellitus, in addition to 50 (17 males and 33 females). Age and gender matched healthy volunteers as control. Results: The study showed that there is a highly statistically significant difference between study and control groups as regard E/é septal and E/ é lateral with (P=0.002) and (P=0.003) respectively. **Conclusion:** The study shows there are statistically significant differences of left ventricular diastolic function by pulsed-wave and tissue Doppler echocardiographic indices according to E/E' septal and lateral in patients with type II diabetes mellitus in comparison to non-diabetics. There are insignificant statistical differences in diastolic functions between diabetic males and females. This study might provide important view about differences in left ventricular diastolic dysfunction in diabetic patients free from hypertension and ischemic heart disease. Recommendations: Diabetic patients should be evaluated for subclinical diastolic dysfunction by Doppler studies as well as good control of diabetes for deceleration of the development of clinical cardiomyopathy, and decreased morbidity and mortality.

**Key words:** Diabetes mellitus, Cardiology, insulin secretion, carbohydrate, diastolic heart failure

#### Introduction

Diabetes mellitus (DM) may be considered as one of the challenges even in the highly developed medical field of the 21st century. It is becoming an epidemic health threat (*Ren and Sowers, 2013*). It affects 350 million people around the world, and the World health organization (WHO) has projected that diabetes deaths will be doubled between 2005 and 2030 (*Battiprolu et al., 2013*).

Diabetes mellitus characterized by hyperglycemia associated with disturbances of carbohydrate, protein and fat metabolism. With absolute or relative deficiencies in insulin secretion and/ or insulin action (*Ojji*, 2011). The disease causes significant organ dysfunction with acute and long term complications that results in diabetes related morbidity and mortality (*Pappachan et al.*, 2013).

Cardiovascular diseases has been singled out as a major cause of death in patients with DM as diabetes increases the risk of developing heart disease by several folds. Heart involvement in diabetes goes beyond the damage to coronary arteries due to the progress of atherosclerotic process. Diabetes and its pathophysiological consequences are able to induce direct alterations and abnormalities in the cardiac muscle functions (*Ciccone et al.*, 2014).

Diabetes may affect the heart in three ways: (a) coronary artery disease due to accelerated atherosclerosis; (b) cardiac autonomic neuropathy; and (c) diabetic cardiomyopathy. Several studies have suggested that diabetes may be associated with left ventricular (LV) structural and functional abnormalities in addition to, and independent of atherosclerosis (*Ojji*, 2011).

The high morbidity and mortality for diabetic cardiomyopathy warrant aggressive clinical management. In addition, the increasing detection of this added cardiac insult is supported by data from epidemiological, molecular as well as diagnostic studies. It is worth to be mentioned that there is increasing evidence of diabetics with abnormalities of left ventricular function in the absence of clinical heart disease and this is what called as diabetic cardiomyopathy (*Medicine update*, 2010).

More recent data have also demonstrated an independent association between diastolic function and DM type 2 where insulin resistance can be one of the important pathophysiological links involved in this association (*Horwich and Fonarow*, 2010). Several studies have suggested that left ventricular dysfunction is one of the earliest signs of myocardial involvement in type 2 diabetes mellitus (T2DM) (*Zabalgoitia et al.*, 2001).

Echocardiography plays a central role in the evaluation of diastolic function, and conventional pulsed-wave (PW) Doppler is usually performed to obtain mitral inflow velocities to assess left ventricular filling. Doppler pattern of impaired left ventricular relaxation, characterized by decreased early and increased late diastolic flow, is an early sign of diastolic dysfunction (*Nagueh et al.*, 2009).

Compared with epidemiological studies on cardiovascular disease (CVD), less attention is given to examining whether disparities in CVD risk management create gender differences among an already high-risk population like those with diabetes. Although differences exist between men and women with T2DM regarding CVD occurrence, gender differences in composite control of cardiovascular risk factors are less understood (*Joni et al.*, *2014*).