A DISSERTATION ON

"LEFT VENTRICULAR STRUCTURAL AND FUNCTIONAL ABNORMALITIES IN TYPE 2 DIABETES MELLITUS"

M.D DEGREE

BRANCH - I

(GENERAL MEDICINE)

MARCH 2007

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

CERTIFICATE

This is to certify that the dissertation titled ***"STUDY OF LEFT VENTRICULAR FUNCTIONAL AND STRUCTURAL ABNORMALITIES IN TYPE 2 DIABETES MELLITUS"*** *submitted by* ***Dr. S.PALANISAMY*** *to the Faculty of General Medicine, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.*

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DECLARATION

I, **Dr. S. PALANISAMY**, solemnly declare that the dissertation titled **"STUDY OF LEFT VENTRICULAR STRUCTURAL AND FUNCTIONAL ABNORMALITIES IN TYPE-2 DIABETES MELLITUS"** has been prepared by me. I also declare, this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other university or board either in India or abroad.

This is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in General Medicine to be held in March 2007.

Place: Madurai **Dr.S.PALANISAMY**

Date:

ACKNOWLEDGEMENT

My sincere thanks to The Dean, ***Dr.S.M.SIVAKUMAR M.S****, for permitting me to use the facilities of Madurai Medical College and Govt. Rajaji Hospital to conduct this study.*

My Professor and Head of the Department of Medicine, Prof. ***NALINI GANESH M.D.,*** *has always guided me, by example and valuable words of advice throughout the conduct of the study and also during my postgraduate course. My sincere thanks to her*

I will ever remain in gratitude to my chief ***Dr.A.AYYAPPAN M.D.,*** *Department of Medicine, not only for guiding me through this study, but also for being my mentor and source of inspiration during the period of my postgraduate training.*

My heartfelt thanks to ***Dr. J. SANGUMANI M.D., Dr. L. JERALD MAJELLAH M.D., Dr. P.R. SHEELA M.D.****,* ***Dr. S. SOMASUNDARAM M.D.,*** *and* ***Dr.RAMAKRISHNAN M.D.*** *for their valuable support and guidance throughout the study and also for making my stay in the unit both informative and pleasurable.*

I express my sincere thanks to ***Dr. ARTHUR ASIRVATHAM, MD., D.Diab., PROF. AND H.O.D., Diab.****, GRH,Madurai for his guidance throughout the study.*

I express my sincere thanks to ***Dr. S. MURUGAN M.D., D.M****., Assistant Professor, Department of Cardiology, GRH,Madurai for his guidance and help.*

*My **family and friends** have stood by me during my times of need. Their help and support have been invaluable to this study.*

*I would grossly fail in my duty if I fail to mention here of my **patients**, who have ungrudgingly borne the pain and discomfort of the investigations. I cannot but pray for their speedy recovery and place this study as a tribute to them and to the numerous others likely affected involved during the study period.*

CONTENTS

INTRODUCTION

The world today is witnessing an epidemic of diabetes mellitus.[1]Globally and nationally, diabetes and its complications has become the most important contemporary and challenging health problem.

It is estimated that there will be more than 200million diabetics in the world within the next 10 years. India has already become the diabetes capital of the world with over 30 million affected patients that is alarmingly just a tip of the iceberg and is expected to touch the 55million mark in 2025.[1]

The impact of diabetes on both the health of the individual and the health care system resides almost entirely in the long term complications of diabetes.

The FRAMINGHAM HEART STUDY revealed marked increase in peripheral arterial disease, congestive heart failure, coronary artery disease, myocardial infarction and sudden death(The risk increases from 1 to 5 fold) in diabetics.[2]

The American Heart Association recently designated DM as a major risk factor for cardiovascular disease along with other major risk factors(smoking,hypertension and hyperlipidemia)[3]

Though DM is associated with a multitude of cardiovascular complications recent studies have suggested structural myocardial involvement termed “DM Cardiomyopathy”[4.] Myocardial involvement in diabetes may occur

relatively early in the course of the disease,[15] initially impairing the diastolic relaxation and when more extensive resulting in decreased myocardial contraction. Prior to the development of symptomatic CHF sub-clinical LV dysfunction (systolic and diastolic) does exist for some time.[5]

Further, increased LV mass has been documented in Type 2 Diabetes even in normotensive individuals at an early stage. LVH is an ominous prognostic sign and independent risk factor for further cardiac events[13] and hence identification of this subset of patients would enable early interventional strategies that could decrease the incidence of cardiac events.

There have been few studies that have evaluated the development of systolic and diastolic LV dysfunction and LV mass in Type 2 DM patients, who are normotensive and have no cardiac symptoms.[11]

The present study was undertaken to make further inroads into this aspect of diabetes that would have far flung implications in management of diabetes as a whole.

AIM OF THE STUDY

- Echocardiographic assessment of left ventricular functional and structural abnormalities in Type 2 DM patients who are normotensive and without any cardiac symptoms.
- To assess the relationship between the duration of diabetes mellitus and the development of LV structural and functional abnormalities

REVIEW OF LITERATURE

Definition:

DIABETES MELLITUS is defined as a syndrome characterized by chronic hyperglycemia, associated with disturbances of carbohydrate, fat and protein metabolism due to absolute or relative deficiency in insulin secretion and/or action.

In view of the wide heterogeneity, Diabetes is regarded as a “syndrome” rather than a disease entity.[1]

Classification:

This classification is based on the pathogenic process that leads to hyperglycemia as opposed to earlier criteria that included the age of onset and type of therapy.[3]

The classification of DM:

1. Type 1 DM (β cell destruction, usually leading to absolute insulin deficiency)

    A: Autoimmune mediated

    B: Idiopathic

2. Type 2 DM (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)
3. Other types:
    - Genetic defects of β cell function characterized by mutation in:
        1. Hepatocyte nuclear transcription (HNF) 4α MODY 1
        2. Glucokinase MODY2
        3. HNF-1α MODY3
        4. Insulin promoter Factor (IPF) 1 MODY4
        5. HNF-1β MODY5
    - Genetic defects in insulin action
        1. Type A insulin resistance
        2. Leprechaunism
        3. Lipoatrophic diabetes
    - Disease of the exocrine pancreas
    - Endocrinopathies
    - Drugs, Toxin induced
    - Infections
    - Other genetic syndromes

4. Gestational Diabetes Mellitus (GDM)

TYPE 1 DIABETES MELLITUS:

This was previously known as Insulin Dependent Diabetes Mellitus (IDDM). These patients require insulin for survival, as the endogenous insulin secretion is almost absent in them. This disease has its onset most often in childhood and adolescence, although it may occur at any age. Though usually abrupt in onset, it can be protracted in its course. Genetic factors, autoimmunity and environmental factors play a major role in the causation and the precipitation of Type1 diabetes.

The auto immune aetiology of the disorder is well recognized by the presence of immune markers, like Islet cell antibodies (ICA), Insulin autoantibodies and antibodies against 64KD antigen.

Type 1 DM comprises of two broad categories, Type 1A and Type 1B. Type 1A diabetes results from autoimmune beta cell destruction, which usually leads to insulin deficiency. Type1B diabetes is characterized by insulin deficiency of unknown aetiology, with lack of immunological markers indicative of autoimmune destructive process of β cell.

Pathogenesis:

Type 1 DM develops as a result of synergetic effect of genetic, environmental and immunological factors that ultimately destroy the β cells. Individuals with a genetic susceptibility have normal cell β cell mass at birth, but begin to lose β cells secondary to autoimmune destruction that occurs over

months to years. The autoimmune process is thought to be triggered by an infectious or environmental stimulus and to be sustained by a beta cell specific molecule. In the majority of the individuals immunological markers appear after the triggering event, but before diabetes become clinically overt. β cell mass then begins to decline and insulin secretion becomes progressively impaired, although normal glucose tolerance is maintained. Features of diabetes do not become evident until a majority (>80%) of β cells are destroyed. At this point, the residual functional β cells still exist, but are insufficient in number to maintain glucose tolerance. The events that contribute to the transition from glucose intolerance to frank diabetes are associated with increased insulin requirements, as might occur during infections or puberty.

Various factors can be attributed to the pathogenesis of Type 1 DM:

1. Genetic factors

Genetic contribution to Type 1DM involves multiple genes. The concordance of Type 1DM in identical twins is between 30-70%[3], indicating that additional modifying factors must be involved in determining whether diabetes develops or not. The major susceptibility gene for Type1DM is located in HLA region on chromosome 6. Most individuals with Type 1 DM have HLA DR3/DR4 halotype. Refinements in genotyping of HLA loci have shown that the halotypes DQA1*0301, DQB1*0302, DQA1*501 and DQB1*0201 have the strongest association with Type 1 DM.

2. Autoimmune factors:

Pathologically, the pancreatic islets are infiltrated with lymphocytes (in a process termed insulitis) due to autoimmunity, leading to destruction of the β cells. As a result, the following abnormalities appear in the immune system;

a. Islet cell autoantibodies
b. Activated lymphocytes in the islets, peripancreatic lymphnodes and the systemic circulation.
c. T lymphocytes that proliferate when stimulated with islet proteins, and
d. Release of cytokines within the insulitis.

3. Immunological markers:

Islet cell autoantibodies are present in the majority (75%) of individuals diagnosed as Type 1DM.This includes antibodies to GAD (Glutamic acid decarboxylase) 65, IA-2/ICA-512 and Islet gangliosides.

4. Environmental factors:

Various environmental factors have been proposed to trigger the autoimmunity in genetically susceptible individuals. They are mainly viral infections (Coxsackie and Rubella), early exposure to bovine milk proteins and nitrosourea compounds.

TYPE 2 DIABETES MELLITUS

Type 2 DM is a heterogenous disorder with a complex aetiology that develops in response to genetic and environmental influences. Central to the development of Type 2 DM are Insulin resistance and Abnormal insulin secretion. Although controversy remains regarding the primary defect, most studies support the view that insulin resistance precedes insulin secretory defects.

Genetic considerations:

Although the major genes that predispose to this disorder have yet to be identified it is clear that the disease is polygenic and multifactorial. The concordance of Type 2 DM in identical twins is between 70-90%[3.] If both parents have Type2DM the offspring have risk approaching 40%.

Pathogenesis:

Type 2 DM is characterized by 3 pathophysiological abnormalities:

1. Peripheral insulin resistance
2. Impaired insulin secretion

and 3. Excessive hepatic glucose production

Peripheral insulin resistance:

In early stages glucose tolerance remains normal despite insulin resistance as the pancreatic β cells compensate by increased insulin output. However as the insulin resistance and compensatory hyperinsulinemia progress, the pancreatic islets in certain individuals are unable to maintain the

hyperinsulinemic state. Thus begins a spectrum from impaired glucose tolerance to overt diabetes mellitus reflecting the progress towards β cell failure.

Insulin resistance results from a combination of genetic susceptibility and obesity. Insulin resistance impairs glucose utilization by insulin sensitive tissues and increases hepatic glucose output, both effects contribute to hyperglycemia. Increased hepatic glucose output and decreased peripheral glucose utilization account for the increased fasting plasma glucose levels and postprandial hyperglycemia respectively. The molecular mechanism of postreceptor defects include (a). Polymorphism in IRS-1 (b)PI-3 kinase signaling defects, which reduces translocation of GLUT4 to the plasma membrane and (c) elevated levels of free fatty acids in obese individuals results in impaired glucose utilization in skeletal muscle, promote glucose production by the liver and impair beta cell function.

Impaired insulin secretion:

The cause of impaired insulin secretion in type 2 DM is unclear. It is hypothesized that this may be due to (a) Islet amyloid polypeptide/amylin. (Amylin has been reported to lower basal and insulin stimulated glycogen synthetase in the muscle and also to inhibit glucose stimulated insulin secretion) (b)Glucotoxicity. Chronic hyperglycemia paradoxically impairs beta cell function. (c) Lipotoxicity. Elevated free fatty acids and dietary fat worsen islet function.

Increased hepatic glucose production

In type2 DM, insulin resistance in the liver reflects the failure of hyperinsulinemia to suppress neoglucogenesis which results in fasting hyperglycemia and decreased glycogen storage by the liver in the postprandial state.

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Risk factors for Type 2 DM:

1. Family history of Diabetes.
2. Obesity(BMI≥25kg/m^2)
3. Habitual physical inactivity
4. Race/Ethnicity
5. Previously identified IFG or IGT
6. History of GDM or delivery of baby>4kg

7. Hypertension(BP≥140/90mmHg)
8. HDL cholesterol level ≤35mg/dl), or TGL level ≥250mg/dl
9. Polycystic ovary syndrome or Acanthosis nigricans
10. History of Vascular disease

Differentiation of Type 1 and Type 2 DM by clinical criteria: [3]

S.No	Type 1 DM	Type 2 DM
1	Onset of disease prior to age of 30yrs	Onset of disease after 30years
2	Lean body habitus	80%obese(elderly individually may be lean)
3.	Requirement of insulin as the initial therapy	May not require insulin therapy initially
4.	Propensity to develop ketoacidosis	Not usually prone for ketoacidosis
5.	Associated with other autoimmune disorders(eg.autoimmune thyroiditis,pernicious anaemia and vitiligo)	Associated with conditions like hypertension, dyslipidemia, PCOD and cardiovascular disease.
6.	Presence of ICA and GAD Antibodies	No autoantibodies

DIAGNOSIS:[3]

- Symptoms of Diabetes plus random* blood glucose concentration ≥11.1mmol/L(200mg/dl)

  or

- Fasting** plasma glucose ≥7mmol/L(126mg/dl)

  or

- 2hr plasma glucose≥11.1mmol/L(200mg/dl)

  during on oral GTT***.

*Random is defined as without regard to time since the last meal.

** Fasting is defined as no caloric intake for at least 8hrs.

*** The test should be performed using a glucose load containing the equivalent of 75g anhydrous glucose dissolved in water; not recommended for routine use.

Long term Complications:

Although chronic hyperglycemia is an important aetiologic factor leading to the complications of DM, four prominent theories have been proposed to explain how hyperglycemia might lead to the chronic complications:

1. Formation of advanced glycosylation end products (AGEs) via nonenzymatic glycosylation of intra and extracellular proteins.
2. Increased metabolism of glucose through the sorbitol pathway by the enzyme Aldose reductase. Sorbitol in turn increases the cellular

osmolality, generates reactive oxygen species and alters the redox potential and thus leads to cellular dysfunction.

3. Increase the formation of DAG (Diacyl glycerol) leading to activation of Protein kinase C which in turn alters the transcription of genes for fibronectin, type-IV collagen, contractile proteins and extracellular matrix proteins.
4. Increased formation of Fructose-6-phosphate through the Hexosamine pathway which may alter the function of nitric oxide synthase or by changes in the gene expression of TGF-β and PAI-1(Plasminogen activator inhitbitor1)

S.No.	Chronic complications of DM	
1.	Macroangiopathy	Coronary artery disease, Cerebrovascular disorder, Peripheral vascular disease
2.	Microangiopathy	Retinopathy, Macular edema, Nephropathy, Neuropathy(Sensory, Motor), Autonomic
3.	Others	Dermatopathy, GIT (gastroparesis, diarrhea),Genitourinary(Uropathy, sexual dysfunction), Infectious, Cataract, Glaucoma

LV STRUTURAL AND FUNCTIONAL ABNORMALITIES

NORMAL LV FUNCTION

The three basic events of the cardiac cycle are

1. LV contraction
2. LV relaxation
3. LV filling.

1. LV Contraction

It comprises of 1.Isovolumic contraction phase extending from closure of mitral and tricuspid valve to the time when pressures in the left and right ventricles exceed the pressures in the aorta and the pulmonary artery 2.Phase of ventricular ejection that begins as the aortic and pulmonary valves open and ends when the ventricular pressures drop rapidly.

2. LV Relaxation

It comprises of i). Protodiastole (Phase of reduced ejection) the period when the ventricular pressures drop very rapidly and ends when the momentum of ejected blood is overcome and aortic and pulmonary valve close. ii). Isovolumic ventricular relaxation: Begins with closure of the aortic and pulmonary valve and ends with the opening of AV valves as ventricular pressure falls below the atrial pressure.

3. Left ventricular filling:

It comprises 1.Rapid filling phase which starts as pressure in the ventricle drops below the left atrial pressure and the mitral valves open. This period of rapid filling ends when pressure in the atrium and ventricle equalize. 2. Diastasis: virtually no flow into the ventricle is seen during this phase 3.Atrial systole (Late diastolic phase).

LV SYSTOLIC FUNCTION: [6]

The determinants of LV systolic function are 1.preload 2.afterload 3.myocardial contractility and 4.heart rate

The specific indices used to evaluate LV systolic function are:

1. Ejection fraction

Ejection fraction is defined as the ratio of the stroke volume to end diastolic volume.

$$EF = EDV - ESV/EDV \times 100(\%)$$

The normal value of LVEF is 55-75%.

2. End systolic ventricular volume/dimension:

ESV is strongly afterload dependent and is relatively independent of preload. It is useful to assess LV function in patients with valvar regurgitation.

3. Other indices:

Include VCF (Velocity of circumferential fibre) shortening, Afterload corrected VCF, Slope of End systolic pressure volume relationship, End systolic

stiffness, Preload recruitable stroke work and the Maximum rate of pressure rise.

LV DIASTOLIC FUNCTION[6]

Assessment of cardiac performance has traditionally focused on systolic function. More recently however diastolic function has been found to play an important role in cardiac morbidity and mortality. Diastolic function is influenced importantly by ventricular structure and composition. However, clinically, four phases of diastolic function need to be distinguished 1.isovolumetric relaxation 2.early rapid diastolic filling (E) 3.slow ventricular filling (Diastasis) and 4. late atrial filling (A).

Diastolic function is influenced by several factors which include 1.myocardial relaxation 2.ventricular filling 3.elastic recoil 4.heart rate and 5.atrioventricular pressure gradient.

Specific indices used to evaluate diastolic dysfunction include:

1. IVRT (Intraventricular isovolumetric relaxation time):

This is the interval from the aortic valve closure to mitral valve opening. Normal: 70-90millisecond

2. Peak mitral flow velocity

Peak mitral flow velocity of early rapid filling wave (E) and Peak velocity of late filling wave (A) due to atrial contraction are expressed as E/A ratio. Normal >1.

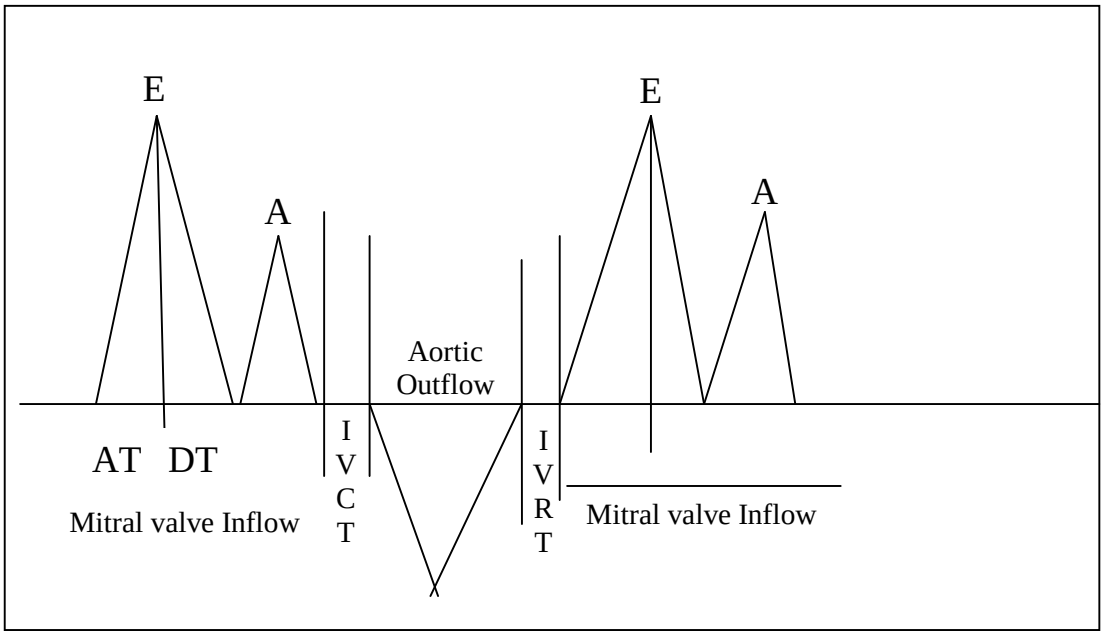
3. Deceleration time (DT):

This is the interval from the peak of the E velocity to extrapolation to baseline. Normal <240ms.

4. Other indices include:

Pulmonary vein flow velocities, tricuspid flow velocities and hepatic vein flow velocities and SVC flow velocities.

NORMAL DIASOLIC FILLING PATTERN



The rate of myocardial relaxation and compliance change with aging, so that, different diastolic filling patterns are expected for different age groups.

Abnormalities of LV systolic function:

This is usually identified on echocardiograhic measurement of Ejection Fraction. EF <55% denotes LV dysfunction.

Abnormalities of LV diastolic function: [6]

1. Diastolic abnormalities:

Characterized by abnormal filling indices, they are commonly identified on echo by prolonged IVRT, however, these patients have no clinical symptoms. In this situation the ventricle is able to compensate for abnormal diastolic function and to maintain a normal level of left ventricular filling pressure.

2. Diastolic dysfunction:

Characterized by increased diastolic filling pressure which may be responsible for the occurrence of dysnoea especially during exercise.

3. Diastolic heart failure:

Associated with clinical signs like PND and orthopnoea.

Echocardiographic classification of diastolic filling[27]

	DT (msec)	IVRT (msec)	MITRAL E/A	PVS2&PVd
Normal	160-240	70-90	1-2	PVS2≥PVd
Impaired Relaxation	>240	>90	<1	PVS2>>PVd
Pseudo normal	160-200	<90	1-1.5	PVS2<PVd
Restrictive filling	<160	<90	>1.5	PVS2<<PVd

The clinical differentiation of the two forms of heart failure is of utmost importance as treatment modalities entirely differ.

LEFT VENTRICULAR MASS

The role of LV mass estimation and diagnosis of LVH in cardiovascular disease management is based on epidemiological research and clinical grounds. In general, heart size increases during infancy and adolescence due to body size enlargement, and at this stage, the gender difference becomes prominent. The physiological factors[8] that contribute to LV mass are:

1. Gender-women have increased parietal hypertrophy response to pressure than men.
2. Ethnicity-some ethnic groups have higher LV mass(African Americans)
3. Obesity

4. Age: LV mass progressively increases with age, particularly parietal thickness. However, **Dannenberg and coworkers** demonstrated that LV mass did not increase with age in a healthy sub-sample of the Framingham study, suggesting that most of the supposed physiological increase is caused by other determinants that include Hypertension, DM with metabolic syndrome, Alcohol consumption, Increased salt intake, Smoking and Increased leisure time physical activity in men, Blood lipid, Pulmonary function and Heart rate.

Echocardiographic measurement of LV mass is generally calculated as the difference between the epicardium delimited volume and the LV chamber volume multiplied by an estimate of myocardial density. Both M mode and 2D

imaging can be employed to calculate LV mass. Despite more than 30 years of use Echocardiograph based LV mass calculation and definition are still variable among Ultrasound technicians around the world. **The Echocardiographic criteria to calculate LV mass in this study was:** [18]

	(RWT)	(LVMI)g/m2
Normal	<0.45	<131(men), <100(women)
Concentric Remodeling	>=0.45	<131(males), <100(females)
Concentric Hypertrophy	>=0.45	>131(males), >100(Females)
Eccentric Hypertrophy	<0.45	>131(males), >100(females)

DIABETES AND CARDIOVASCULAR DISEASE

Diabetes mellitus is an independent risk factor for cardiovascular disease (CVD). In the **FRAMINGHAM STUDY** the risk of CVD for diabetic subjects at baseline was two fold higher in men and three to four fold for women after adjustment for other risk factors such as dyslipidemia and hypertension. More recently **NHANES1 study** also showed that the diabetic population was twice as likely to develop CAD as the nondiabetic population with excess mortality .

The **MRFIT STUDY** shows that men with diabetes had an absolute risk of death due to CAD more than three times than the nondiabetic cohort.

In the six nation **OASIS study**[6], diabetic patients presenting with unstable angina or Non Q MI had increased rate of stroke, CHF and death during index hospitalization compared with the non-diabetic group.

In the Finnish contribution to **WHO MONICA** (World Health Organization Multinational Monitoring of Trends and Determinants of Cardiovascular Disease) project, the 1 year mortality was 38% higher for diabetic men and 86% higher for women.

In view of the above, studies have been undertaken in recent times to identify structural and functional abnormalities in normotensive diabetics who have no cardiac symptoms. Most of the recent studies identified changes in LV mass and LV systolic and diastolic function indices even before the patients are symptomatic.

The main factors that contribute to the increased incidence of cardiovascular disease in DM are: [1]

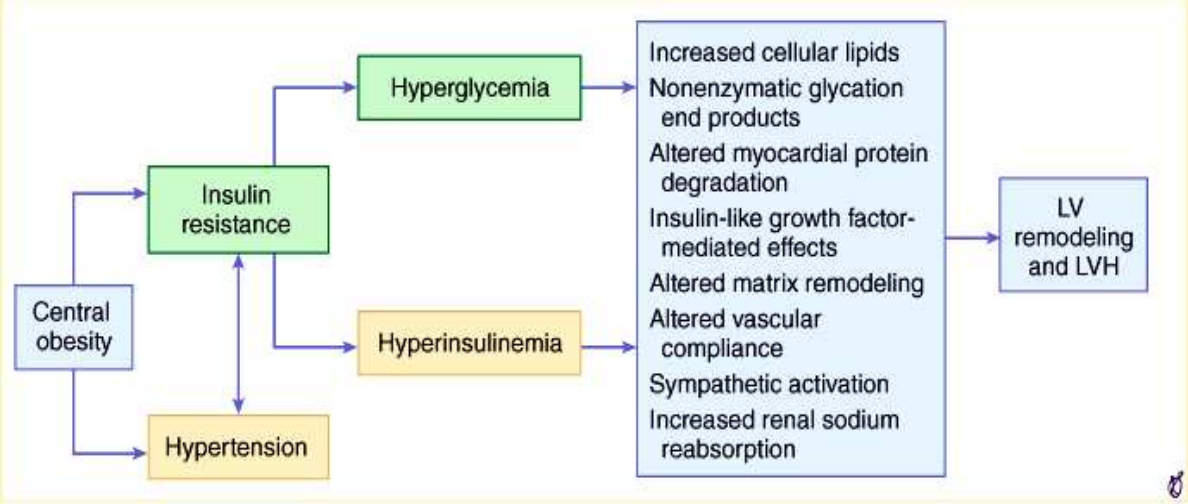
1. The acceleration of atherosclerotic process leading to macrovascular disease.
2. Development of specific cardiomyopathy
3. Progressive microvascular disease
4. Development of autonomic neuropathy

Noninvasive methods have confirmed that fibrosis is a key feature of the heart of diabetic patients without evident cardiac disease. Increased level of collagen in diabetics have been associated with changes in left ventricular diastolic function.[11] Chronic hyperglycemia leads to the formation of AGE's that modify the extracellular matrix, resulting in inelasticity of the vessel wall and could interfere with myocardial function as well.[6] These coupled with abnormal myocardial calcium handling result in poor elastic recoil, leading to impairment in early rapid diastolic filling(E) manifest by prolonged IVRT and DT, and increased Mitral (A) velocity.

In the setting of insulin resistance, there is release of free fatty acids from adipose tissue into the plasma. FFA becomes the dominant fuel for myocardial energy in the form of free fatty acid oxidation within cardiac myocytes. In addition, the rise in plasma free fatty acids leads to a decrease in glycolysis and

glucose oxidation in these cells. Free fatty acid oxidation is a less efficient means of generating adenosine triphosphate than glucose oxidation thus contributing to chronic left ventricular dysfunction.

The impact of glucose intolerance and insulin resistance on cardiac structure and function is as follows:



MATERIALS AND METHODS

All patients included in the study were taken from the Diabetology department of Govt. Rajaji Hospital, Madurai.

This is a case control cross sectional study. The study period was from August –2005 July 2006. The diagnosis of the cases was based on clinical features and WHO criteria for DM. The total number of patients in the study group were 60, this includes 28 males and 32 females. The study group was further subdivided into three groups based on the duration of Diabetes.

GROUP I: 0-5YEARS

GROUP II: 6-10YEARS

GROUP III: >10YEARS

The control group was taken from the Outpatient Dept of Medicine and Inpatients admitted for other ailments. This group was designated as GROUP IV. Total number of controls was 40, which included 20 males and 20 females. All cases and controls were within the age of 40-60 years. Both cases and controls were examined and recruited in the study in the same time period. All subjects gave informed consent for their participation in the study.

Inclusion criteria:

1. All cases of Type 2DM diagnosed by WHO criteria
2. Age: 40-60 years
3. BP: <130/85 (at least 3 recordings with the highest recording taken into consideration)

Exclusion criteria were

1. Systemic Hypertension(BP>140/90)
2. Ishaemic heart disease(abnormal E.C.G. and RWMA on Echo)
3. CHF
4. Congenital or Acquired Valvular Heart Disease
5. CRF
6. Age>60yrs
7. cardiac signs and symptoms(exertional dysnoea, chest pain, palpitation, raised JVP)
8. PDR/NPDR and
9. Microalbuminuria.

Echocardiography:

Patients were evaluated by 2D and Doppler Echocardiography. All examinations were performed using a ALOKA SSD 2000 machine 2.5Mhz transducer. The following were registered on assessment:

1.Ejection Fraction2.LV mass 3.Mitral Early filling velocity (E), Mitral late atrial filling velocity (A),E/A was then derived4.IVRT

and 5.DT.

Operators blinded to the diabetes diagnosis of the patients performed all Echocardiographic measurements.

Computer Analysis of data was done using the software epidemiological information package – 2002 developed by **Centre for Disease Control and Prevention, Atlanta** in collaboration with WHO.

Chi – square test was used for tests of significance.

A. Comparison of Parameters in Diabetic Group (cases) and non diabetic group (Cantnoes)

Table 1: AGE

Age Group	Diabetic		Non-Diabetic	
	No	**%**	**No**	**%**
40 – 44	14	23.3	10	25
45 – 49	14	23.3	9	22.5
50 – 54	9	15	9	22.5
55 – 59	14	23.3	8	20
60 & above	9	15	4	10
Total	**60**	**100**	**40**	**100**
Mean	50.25		50.45	
S.D.	6.95		6.06	
p	0.9494 (Not Significant)			

Table 2: SEX

Sex	Diabetic		Non-Diabetic	
	No	**%**	**No**	**%**
Male	28	46.7	20	50
Female	32	53.3	20	50
p	0.9024 (Not Significant)			

Table 3: EF %

EF%	Diabetic		Non-Diabetic	
	No	**%**	**No**	**%**
Normal	46	76.7	36	90
Abnormal	14	23.3	4	10
Mean	60.56		63.82	
S.D.	7.53		7.18	
p	0.1514 (Not Significant)			

Table 4: LV Mass (gm/m^2)

LV Mass (gm/m^2)	Diabetic		Non-Diabetic	
	No	**%**	**No**	**%**
Normal	39	65	34	85
Abnormal	21	35	6	15
Mean	98.77		97.59	
S.D.	24.65		8.45	
p	0.045 (Significant)			

Table 5: Deceleration Time

Deceleration Time	Diabetic		Non-Diabetic	
	No	%	No	%
Normal	34	56.7	28	70
Abnormal	26	43.3	12	30
Mean	205.65		207.6	
S.D.	43.74		32.1	
p	0.2561 (Not Significant)			

Table 6: IVRT

IVRT	Diabetic		Non-Diabetic	
	No	%	No	%
Normal	21	35	22	55
Abnormal	39	65	18	45
Mean	101.65		93.2	
S.D.	25.8		17.5	
p	0.0762 (Not Significant)			

Table 7: E/A Ratio

E/A Ratio	Diabetic		Non-Diabetic	
	No	**%**	**No**	**%**
Normal	25	41.7	28	70
Abnormal	35	58.3	12	30
Mean	0.94		1.15	
S.D.	0.28		0.23	
p	0.0099 (Significant)			

Table 8: Pulse Rate per Minute

Pulse Rate	Diabetic		Non-Diabetic	
	No	%	No	%
Normal	46	76.7	40	100
Abnormal	14	23.3	-	-
Mean	90.55		81.7	
S.D.	12.65		5.52	
p	0.0027 (Significant)			

B. Comparison of Parameters within Diabetic Group according to duration of diabetics – I) 1 to 5 years II) 6-10 years III) More than 10 years

Table 9: AGE

Age Group	I		II		III	
	No	**%**	**No**	**%**	**No**	**%**
40 – 44	5	25	6	30	3	15
45 – 49	4	20	5	25	5	25
50 – 54	2	10	3	15	4	20
55 – 59	7	35	3	15	4	20
60 & above	2	10	3	15	4	20
Total	**20**	**100**	**20**	**100**	**20**	**100**
Mean	50.5		48.7		51.9	
S.D.	7.4		7.1		6.3	
p	0.5218					

Table 10: Sex and Duration if Diabetes

Sex	I		II		III	
	No	**%**	**No**	**%**	**No**	**%**
Male	9	45	9	45	10	50
Female	11	55	11	55	10	50

'p' Value Between

I & II - 0.7506 (Not Significant)

I & III - 1.000 (Not Significant)

II & III - 1.000 (Not Significant)

Table 11: EF% and duration of Diabetes

EF%	I		II		III	
	No	%	No	%	No	%
Normal	18	90	15	75	13	65
Abnormal	2	10	5	25	7	35
Mean	60.42		62.7		58.6	
S.D.	6.1		9.6		6.2	

'p' Value Between

I & II - 0.2763 (Not Significant)

I & III - 0.0636 (Not Significant)

II & III - 0.73 (Not Significant)

Table 12: LV Mass (gm/m^2) and duration of Diabetes

LV Mass	I		II		III	
	No	**%**	**No**	**%**	**No**	**%**
Normal	17	85	13	65	9	45
Abnormal	3	15	7	35	11	55
Mean	86.5		98.8		111.0	
S.D.	19.7		30.2		16.5	

'p' Value Between

I & II - 0.2733 (Not Significant)

I & III - 0.0203 (Significant)

II & III - 0.3403 (Not Significant)

Table 13: Deceleration Time and duration of Diabetes

Deceleration Time	I		II		III	
	No	%	No	%	No	%
Normal	12	60	11	55	11	55
Abnormal	8	40	9	45	9	45
Mean	192.8		212.0		212.2	
S.D.	48.7		49.5		39.7	

'p' Value Between

I & II - 1.00 (Not Significant)

I & III - 1.00 (Not Significant)

II & III - 0.7506 (Not Significant)

Table 14: IVRT and duration of Diabetes

EF%	I		II		III	
	No	%	No	%	No	%
Normal	6	30	7	35	8	40
Abnormal	14	70	13	65	12	60
Mean	108.1		99.5		97.4	
S.D.	20.4		31.3		24.6	

'p' Value Between

I & II - 1.00 (Not Significant)

I & III - 0.74 (Not Significant)

II & III - 1.00 (Not Significant)

Table 15: E/A Ratio and duration of Diabetes

E/A Ratio	I		II		III	
	No	%	No	%	No	%
Normal	10	50	8	40	7	35
Abnormal	10	50	12	60	13	65
Mean	1.0		0.94		0.88	
S.D.	0.3		0.29		0.27	

'p' Value Between

I & II - 0.7506 (Not Significant)

I & III - 0.5223 (Not Significant)

II & III - 1.00 (Not Significant)

Table 16: Pulse Rate per minute and duration of Diabetes

Pulse Rate	I		II		III	
	No	%	No	%	No	%
Normal	16	80	16	80	14	70
Abnormal	4	20	4	20	6	30
Mean	88.2		89.4		94.1	
S.D.	12.1		13.2		12.4	

'p' Value Between

I & II - 0.6526 (Not Significant)

I & III - 0.715 (Not Significant)

II & III - 0.715 (Not Significant)

C. Comparison of parameters within the study group(diabetics) according to Sex

Table 17: Relationship between sex and LV mass

LV Mass	Male		Female	
	No	**%**	**No**	**%**
Normal	24	85.7	15	46.9
Abnormal	4	14.3	17	53.1
Mean	97.88		99.54	
S.D.	26		23.79	
p	0.004 (Significant)			

Table 18: Relationship between sex and E/A ratio

E/A	Male		Female	
	No	**%**	**No**	**%**
Normal	13	46.4	12	37.5
Abnormal	15	53.6	20	62.5
Mean	0.948		0.9365	
S.D.	0.303		0.272	
p	0.6618 (Not Significant)			

Table19: Relationship between sex and pulse rate

Pulse Rate	Male		Female	
	No	**%**	**No**	**%**
Normal	25	89.3	21	65.6
Abnormal	3	10.7	11	34.4
Mean	85.5		95.0	
S.D.	11.76		11.88	
p	0.0635 (Not Significant)			

STATISTICAL ANALYSES

This study was a cross sectional case control study conducted in 60 cases of Type2 DM who satisfied inclusion criteria and 40 age and sex matched controls. The mean age of cases was 50.25 years and controls 50.45years. Of the 60 cases 28(46%) were males and 32(53.3%) were females. Of the 40 controls, 20 were males and 20 were females.

The cases were divided into three groups based on the duration of diabetes. Group I comprising those with diabetes of 0-5 yr duration while Groups II and III comprising those with duration of 5-10yrs and >10yrs respectively. The number of cases in each group was 20.

The mean age of Group I patients was 50.5yrs. Of the 20 patients in the Group,9 were males and 11 were females.

The mean age of Group II patients was 48.7yrs. Of the 20 patients in the Group, 9 were males and 11 were females.

The mean age of Group III patients was 51.7yrs. Of the 20 patients in the group, 10 were males and 10 were females.

In this study, regarding EF <55% considered to be systolic dysfunction. E/A ratio <1, IVRT >90msec and DT >240msec taken as an abnormal diastolic dysfunction.

Regarding LV Mass male >131gm/m^2 and female >101gm/m^2 taken as an increase LV Mass.

Observations of EF revealed that abnormalities were present in 10% of Group I, 25% of Group II and 35% of Group III while only 10% of the control group(Group IV) showed abnormalities.

Observations of LV mass revealed that abnormalities were present in 15% of Group I, 35% of Group II and 55% of Group III while only 15% of the control group(Group IV) showed abnormalities.

Observations of DT revealed that abnormalities were present in 40% of Group I, 45% of Group II and 45% of Group III while 30% of the control group (Group IV) showed abnormalities.

Observations of IVRT revealed that abnormalities were present in 75% of Group I, 65% of Group II and 60% of Group III while 45% of the control group (Group IV) showed abnormalities.

Analysis of E/A ratios revealed that abnormalities were present in 50% of Group I, 60% of Group II and 65% of Group III. 30% of GroupIV (controls) also revealed abnormalities.

It was observed that a resting pulse rate >100 was observed in 20% of Group I and II and 30% of Group III cases while the pulse rate was within the normal range in all controls.

DISCUSSION

In the study, it was observed that 35% of diabetics (cases) and 15% of non-diabetics (controls) had increased LV mass, ('p' < 0.045) which is statistically significant**.** This is in conformity with other studies as shown below.

Studies **by Hirayama et al** [13] observed the increased incidence of LV mass among diabetics (normotensive and asymptomatic) than non-di abetics. **Dawson et al**[11] observed that the prevalence of LVmass abnormalities was 71% among diabetics compared to 35% in our study, this may be due to non exclusion of hypertensives in the study. **Nielsen et al**[16] observed that increased LV mass was found in 51% of diabetics.

Intragroup analyses of cases revealed that Increased LV mass was seen in 15% of Group I, 35% of Group II and 55% of Group III. There was statistically significant association between Group I and Group III (P < .0203). This indicates that the development of increased LV mass is dependent on the duration of Diabetes.

With regard to EF, 23.3% of diabetics and 10% of non diabetics had abnormal EF.This was found to be statistically insignificant. (p<0.1514). This is

in conformance with other studies **Hiroyoshima et al, Siwach et al**[4]**, Saner et al**[19]. However studies by **Annonu et al**[14] observed that diabetics had low EF, however the study group included the presence of complications of diabetes which were excluded in our study. Further **Oirko et al**[15] also observed low EF in diabetics. Thus studies regarding EF abnormalities in DM have observed varying results which need to be further investigated.

Observations of IVRT revealed that 65% of cases and 45% of controls show abnormalities. However this was not statistically significant.(($p<0.0762$)

Observations of DT revealed that 43.3% of cases and 30% of controls show abnormalities which was found to be statistically significant.($p <0.2561$)

Observations of E/A ratio revealed that 58.3% of cases (diabetics) and 30% of controls showed abnormalities, which was found to be statistically significant. ($p<0.0099$).

The observations on IVRT,DT and E/A ratio are in conformance with the study by **Siwach et al.** wherein 68% of diabetics had E/A <1 compared to 58.3% in our study Most other studies performed to analyse diastolic function abnormalities have taken into account E/A ratio as the single parameter of diastolic function. **Spiro Qirko et al,** and **Elizi et al**[12] observed values of E/A<1 in 65.8% and 68.9% of diabetes respectively that was statistically significant in

relation to the controls. This infers that E/A ratio abnormality is an indicator of diastolic dysfunction in diabetics. However the reason for the statistically insignificant values of DT and IVRT abnormalities in diabetics are not known. Diastolic function abnormalities occur early in the course of disease. This is evident by the comparison of E/A ratios in Group I and Group III. Which shows 50% of Group I and 65% of Group III had E/A<1 that was statistically insignificant. ($p<0.5223$).**Bonitio et al**[20] and **Spiro Qirko et al** also observed the same in their studies.

Interestingly, observations of our study revealed increased resting pulse rate in diabetics that was subject to statistical analysis. It was observed that 23.3% of cases (diabetics) and none of controls had increased resting pulse rate which was statistically significant.($p<0.0027$). This was earlier documented by studies by **Atheros et al**[17] and **Saner et al**. The increase in resting pulse rate is probably due to diabetic autonomic neuropathy that was not excluded in our study.

Further observations of LV mass between males and females revealed that 14.3% of diabetic males and 53.1% of diabetic females had increased LV mass which was statistically significant. (p,0.004). This reflects the increased (four fold) cardiovascular mortality in diabetic females compared to males (two fold)

The occurrence of structural and functional abnormalities in Type 2 DM as observed in our study clearly state the importance of Echocardiographic assessment(screening) of all Type 2 DM patients even in the absence of cardiac symptoms. This is feasible as ECHO is easily available in our setup.

LIMITATIONS

1. The study was restricted to hospital patients, so its relevance to the general population is unknown.

2. Patients with DM usually have silent ischemia and this factor was not taken into account in the study.

3. The study is subject to measurement error, subject error and instrument error, though carefully designed.

4. Ambulatory BP could not be done this may affect the study group to some extent.

5. Smoking, obesity and dyslipidemia were not excluded from the study group, this may have some influence on LV mass [9].

The limitations however do not invalidate the main findings of the study.

SUMMARY

Echocardiographic assessment of diabetic non-diabetic group revealed the following findings:

1. In diabetic, systolic function not significantly affected when compare to non-diabetic.
2. Diabetic have increase LV Mass than non-diabetic.
3. In diabetes, females have increase LV Mass than male.
4. The development of LV Mass in diabetic depend upon the duration of illness.
5. IVRT, DT not significantly affected in diabetic when compare to diabetic.
6. E/A ratio significantly affected between diabetic & non-diabetic.
7. In diabetes, IVRT, DT & E/A ratio not significantly affected according to the duration of illness.
8. Diabetic have increase resting pulse rate

CONCLUSIONS

Echocardiographic observation of Type 2 DM patients who are normotensive and have no cardiac symptoms revealed:

- Increased LV mass compared to controls, that is well correlated with the duration of diabetes and with a female preponderance
- LV diastolic dysfunction compared to controls, which does not correlate with the duration of diabetes mellitus, reflecting the occurrence of dysfunction early in the course of disease.
- LV systolic function analyzed through EF is not significantly affected in diabetics.

BIBLIOGRAPHY

1. A.P.I. Textbook of Medicine,6th edition.
2. Plouin IF. The importance of Diabetes as a Cardiovasuclar risk factor.Int J.Clinic Pract.Suppl 2000(110):3-8.
3. Harrisons Principles of Internal Medicine,16th edition.
4. JIACM 2002;3(2):164-8 Echocardiographic Doppler assessment of cardiac function in patients of Type 2 DM
5. Ethn Dis 2005. Autumn;15(4)635-40, LV dysfunction in Type 2 DM without Cardiac symptoms.
6. Braunwald's Heart Disease A Text Book of Cardiovascular Medicine,7th edition.
7. Hurst Volume2,10th edition;2019
8. Joslins Diabetes Mellitus,14th edition 989
9. Echocardiographic based LV mass estimation, Murilo Foppa et al. Cardiovascular Ultrasound 2005,3:17
10. LV function in Type 2 DM in patients without Cardiac symptoms in Zaria, David SO et al.
11. Epidemiology of LVH in Type 2 DM, Dawson A et al. Diabetolgia 2005 Oct;48(10)
12. Reduced LV diastolic function in asymptomatic patients with Type 2 DM, Elizi et al.PMID15648228

13. Determination of LVmass by echocardiography in normotensive Diabetic patients. Hirayama et al. PMID11194283
14. LV systolic and diastolic functional abnormalities in asymptomatic patients with Type 2 DM, Annonu AK et al.PMID 11547274
15. Type 2 DM as an independent predictor of asymptomatic LV diastolic dysfunction, Spiro Qirko et al, Clinical Science 2005;46(2)225-231
16. LVH in Type 2 DM patients with and without Diabetic nephropathy, Nielsen et al. PMID 11547254
17. LV systolic and diastolic function in normotensive Type1 diabetic patients with or without autonomic neuropathy, Athyros et al. PMID12832295
18. Feigenbaumis manual of Echocardiography.6th edition,149
19. Saner H et al. No evidence for systolic and diastolic dysfunction in selected patients with long term Type 1 DM, PMID 10937927
20. Di Bonito et al. Diastolic dysfunction in patients with Type 2DM of short duration.
21. Poirier et al. Diastolic dysfunction in normotensive men with well controlled Type 2 DM.
22. Anderson et al. Prevalence of dysfunction in normotensive men with well controlled Type 2 DM.AMJ. Cardiol.2001:87;320-323
23. Vanninen et al. A study of diastolic dysfunction in Type 2 DM
24. Sampson et al. Association between LVH and erythrocyte sodium lithium exchange in normotensive subjects with and without Type 2 DM, Diabetolgia 1995; 38;454-460
25. Hill DJ et al. Insulin as a growth factor; Pediatr Res 1985;19:879-886

26. Ohya et al. Hyperinsulinemia and LV geometry in worksite population in Japan.Hypertension 1996;27;729-734
27. The Echo manual JAE. K.OH., 2nd Edition
28. Nielsen FS, et al; Beneficial impact of ramipril on left ventricular hypertrophy in normotensive nonalbuminuric Type2 DM patients. Diabetes Care 1998; 21; 804-809
29. DeMaria, et al; Doppler echocardiographic evaluation of diastiolic dysfunction. Cliculation.1991; 84(3 Suppl); 1288-95
30. Williams et al; Fasting insulin and left ventricular mass in hypertensives and normotensive controls. Cardiology. 1992; 81:207-212

TARGET ORGAN ABNORMALITIES IN TYPE 2 DIABETES MELLITUS

Name : Sl. No:

Age : IP.No :

Sex : OP.No :

Duration of Diabetes:

Complaints		**General Examination**		**Investigations**	
Giddiness		Pallor		Urine Albumin	
Palpitation		Jaundice		Hb	
Breathlessness		Cyanosis		ESR	
Chest discomfort		Clubbing		Blood Sugar	
Headache		LNE		Urea	
Vertigo		Pedal oedema		Sr. Creatinine	
Weakness		Pulse rate /min		Sr. Cholesterol	
Dec. in work performance		Peripheral pulse		**ECG**	
Swelling of Legs		BP Rt UL -mmHg		HR	
Bleeding Nose		Lt UL -mmHg		PR	
Seizures		Rt LL -mmHg		QRS QT	
Sexual Dysfunction		**CVS**		AXIS	
Others		Apical Impulse		ST- T Segment	
		JVP		Q Waves	
Personal History		Precardium Pulsations			
Smoker		Epiugatric Pulsations			
Alcholic		S1			
Thyroid		S2			
Family History		Added sounds			
DM		Murmur			
HT		RS			
CAD		Breath Sounds			
Past History		Added Sounds			
DM		**Abdomen**			
TIA					
CVA		**CNS**			

ECHO CARDIOGRAPHY

DIASTOLIC FUNCTION INDICES

IVRT	Mitral E	m/s	A	m/s	E/A
	Tricuspid E	m/s	A	m/s	E/A

Deceleration Time (DT)

SYSTOLIC FUNCTION INDICES

IVS d		LVPW d		LVID d	
IVS s		LVPW s		LVID s	

EF % LV Mass

Valves

Mitral Tricuspid

Aortic

RETINOPATHY

MICROALBUMINURIA

CT SCAN

Diagnosis at presentation

MASTER CHART

Sl.No	GROUP	SEX	AGE	DURATION	EF%	LV MASS	DECE.TIME	IVRI	E/A	PE	TYPE
1	I	2	55	1	56	72.28	240	110	0.635	104	A
2	I	2	40	3	58.3	69.81	140	107	0.721	100	A
3	I	1	60	3	66	107.33	246	142	0.9	76	A
4	I	1	60	5	66	61.61	242	139	0.88	92	A
5	I	1	40	1	55	64.86	178	110	1.54	76	A
6	I	1	59	3	63	124.4	150	110	1.16	80	A
7	I	2	50	1	64	71.76	135	82	1.11	80	A
8	I	2	45	1	50	104.16	241	98	0.823	108	A
9	I	2	58	4	52	80.98	245	99	0.789	90	A
10	I	2	55	4	55	112.19	244	133	0.783	90	A
11	I	2	48	1.5	60	81.92	121	89	1.11	92	A
12	I	2	46	1	56	96.96	167	110	1.13	80	A
13	I	1	40	4	57	68.09	160	78	1.68	110	A
14	I	1	55	4.5	59	59.63	247	139	0.623	78	A
15	I	1	40	1	62	62.12	146	130	1.261	86	A
16	I	1	51	3	64	102	138	87	1.11	78	A
17	I	1	55	4	63	94.21	245	112	0.86	76	A
18	I	2	58	5	58	110.21	241	117	0.58	110	A
19	I	2	42	2	76	92.11	160	86	1.12	80	A
20	I	2	46	3	68	94.2	170	84	1.26	78	A

21	II	2	42	8	73	54	149	75	85	90	A
22	II	1	45	6	72	132.4	242	110	0.8	98	A
23	II	1	60	7	75	65.5	230	117	0.68	82	A
24	II	1	42	6	69	135.4	248	100	1	80	A
25	II	2	50	6	55	89.88	206	92	1.17	78	A
26	II	1	60	8	59	84	244	153	0.66	112	A
27	II	1	60	9	62	126.6	242	105	0.605	80	A
28	II	1	57	6	55	108	180	16	1.22	80	A
29	II	1	50	6	74	102	120	90	1.14	110	A
30	II	2	45	7	50	115.4	241	126	0.9	90	A
31	II	2	45	9	77	64.45	230	125	0.779	82	A
32	II	2	56	6	66	71.48	246	111	0.793	90	A
33	II	2	40	6	52	113.52	244	139	0.75	92	A
34	II	2	40	8	64	116.26	203	71	1.16	110	A
35	II	2	52	9	54	141.66	245	135	0.5	112	A
36	II	2	41	7	58	78	132	82	0.9	80	A
37	II	2	55	7	51	153	244	112	0.8	96	A
38	II	2	42	8	77	63.85	160	89	1.75	82	A
39	II	1	45	9	50	60.84	224	61	1.1	68	A
40	II	1	47	8	60	100	210	80	1.2	75	A
41	III	1	50	16	50	133.36	121	53	1.16	80	A
42	III	2	42	11	71	123.42	242	114	0.631	100	A
43	III	1	60	13	53	70.55	263	107	0.581	80	A

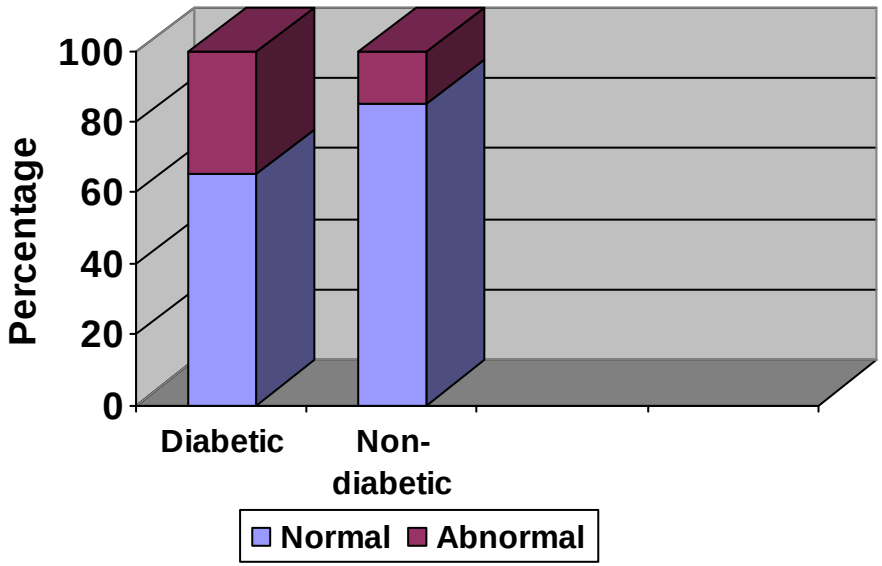
44	III	1	58	12	59.5	114.77	244	95	0.557	80	A
45	III	1	55	14	52	144.57	248	150	0.879	100	A
46	III	1	60	14	63	90.9	170	110	0.54	100	A
47	III	2	42	11	52	109.07	241	110	0.616	107	A
48	III	2	60	14	51	105.45	170	100	1.36	90	A
49	III	2	52	16	64	111.44	178	43	0.818	120	A
50	III	2	49	15	59	120.2	180	76	1.3	105	A
51	III	1	54	13	55	94	247	112	0.84	82	A
52	III	1	47	11	68	105.7	190	84	1.21	78	A
53	III	1	60	16	53	104.7	250	120	0.58	94	A
54	III	1	46	14	58	101.2	260	114	0.681	84	A
55	III	1	44	13	60	122	194	84	1.1	79	A
56	III	2	48	15	64	115.7	178	81	1.21	110	A
57	III	2	56	17	58	120	236	117	0.86	100	A
58	III	2	57	11	67	94	190	78	1.12	86	A
59	III	2	45	15	62	126	194	89	0.85	102	A
60	III	2	53	14	53	112	247	111	0.789	105	A
61	IV	2	41		72	84.12	140	86	1.16	80	B
62	IV	2	44		69	98.1	178	76	1.36	78	B
63	IV	2	59		60	105.76	246	117	0.856	76	B
64	IV	2	60		58	94.7	242	115	0.78	90	B
65	IV	2	49		64	102.7	196	74	1.47	77	B
66	IV	1	40		77	94.8	199	84	1.17	78	B

67	IV	1	48		68	86.7	184	76	1.26	80	B
68	IV	1	60		60	79.06	241	117	0.96	84	B
69	IV	1	53		71	107	211	94	1.24	82	B
70	IV	1	44		74	97.06	194	76	1.47	74	B
71	IV	2	47		62	104.07	210	90	1.26	80	B
72	IV	2	55		58	96.7	247	119	0.96	81	B
73	IV	2	54		62	84.56	199	83	1.34	84	B
74	IV	2	42		69	96.55	187	76	1.47	81	B
75	IV	2	48		59	104.37	210	84	1.12	83	B
76	IV	1	51		62	102.04	217	82	1.35	78	B
77	IV	1	40		74	91.7	196	77	1.4	72	B
78	IV	1	60		55	111.07	257	130	0.856	90	B
79	IV	1	55		67	87.07	241	111	0.9	80	B
80	IV	1	50		55	93.7	194	69	1.2	83	B
81	IV	2	45		67	92.7	104	76	1.34	87	B
82	IV	2	51		54	109	242	109	0.857	87	B
83	IV	2	55		58	87.07	187	89	1.41	69	B
84	IV	2	44		74	105.06	194	67	1.07	77	B
85	IV	2	49		71	93.6	196	87	1.34	84	B
86	IV	1	54		64	107.06	184	81	1.12	78	B
87	IV	1	49		62	91.07	196	89	1.05	76	B
88	IV	1	55		52	106.07	241	116	0.76	82	B
89	IV	1	44		66	98.6	187	84	1.4	78	B

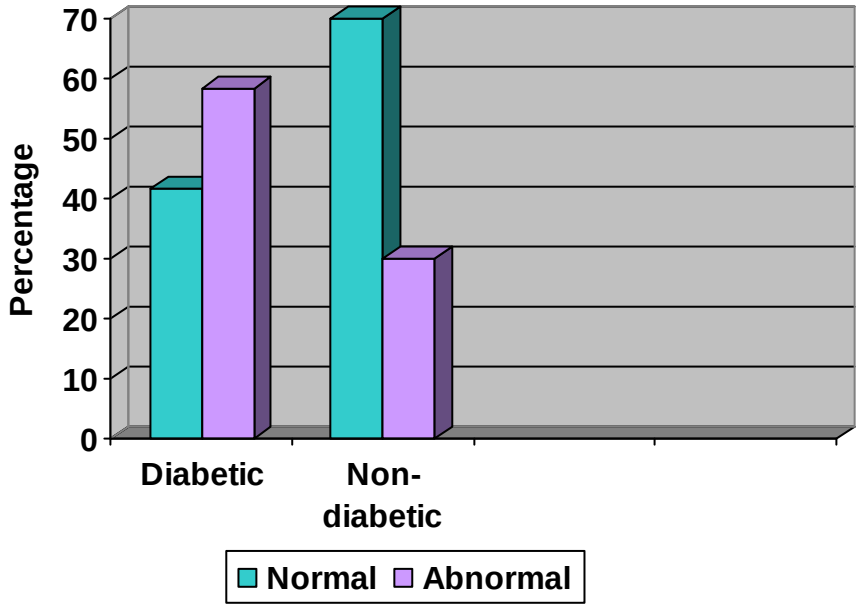
90	IV	1	58		51	112.7	257	120	0.78	96	B
91	IV	2	54		58	96.7	187	83	1.4	79	B
92	IV	2	43		72	79	189	91	1.26	84	B
93	IV	2	47		67	99.99	197	78	1.313	80	B
94	IV	2	56		52	98.6	241	120	0.87	92	B
95	IV	2	49		70	97.57	196	95	1.4	78	B
96	IV	1	50		72	106.3	211	93	1.15	82	B
97	IV	1	58		55	107.6	257	123	0.96	84	B
98	IV	1	53		58	94.67	216	94	1.3	87	B
99	IV	1	44		72	101.07	187	84	1.15	90	B
100	IV	1	60		62	97.54	247	113	0.678	87	B

A – Cases, B- Controls, 1 – Male, 2-Female, Gr. I - Cases 0-5Years, Gr. II – Cases 6-10 Years, Gr.III – Cases More than 10 Years. Gr. IV – Controls.

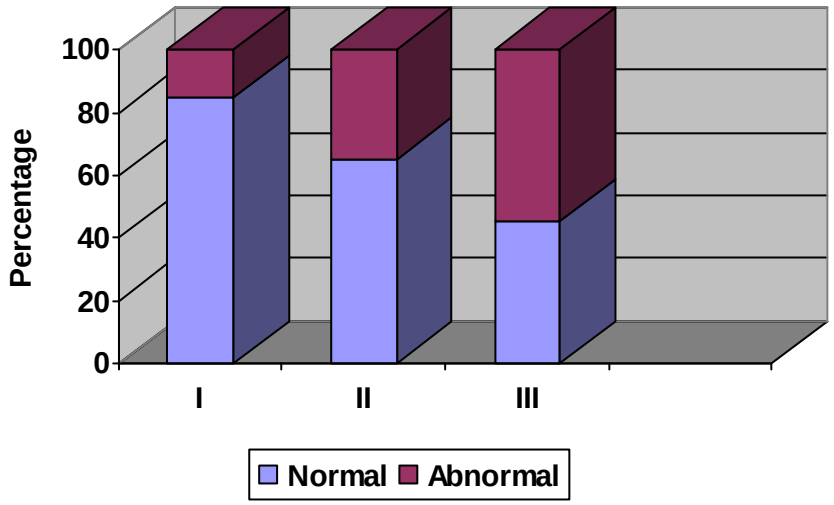
Comparison of Abnormal LV Mass in cases and control



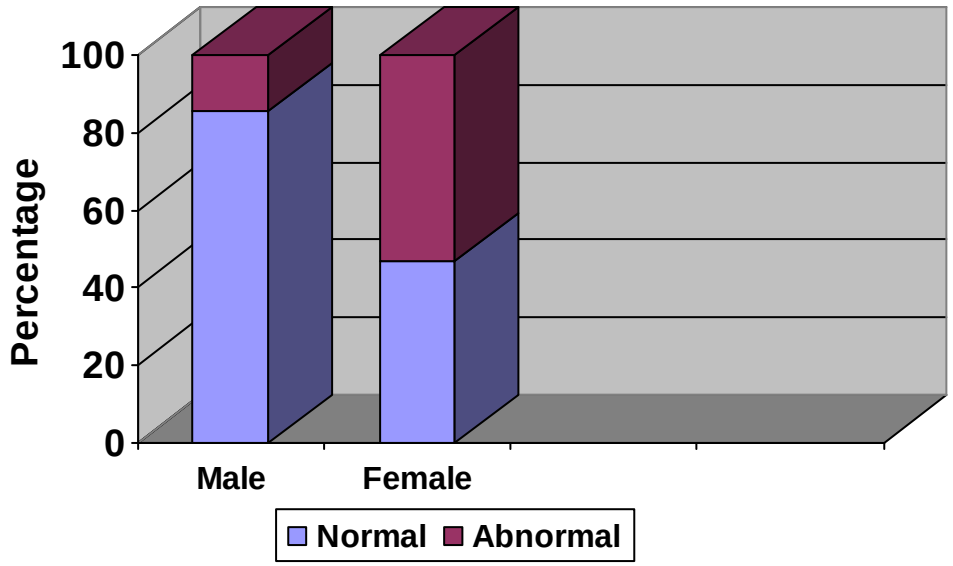
Comparison of Abnormal E/A Ratio in cases and controls

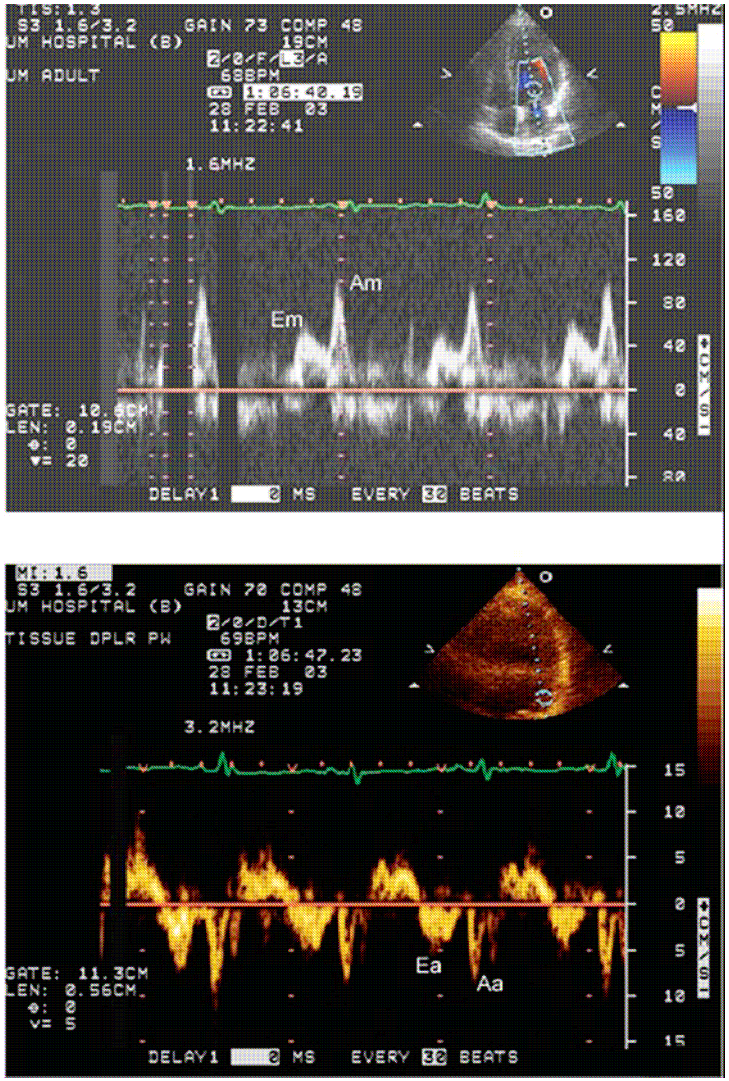


LV Mass (gm/m^2) and duration of Diabetes



Relationship between Sex and LV Mass in cases





Mitral flow velocity and Doppler tissue in patient with diastolic dysfunction and impaired relaxation : Brawnwald 7th 2005

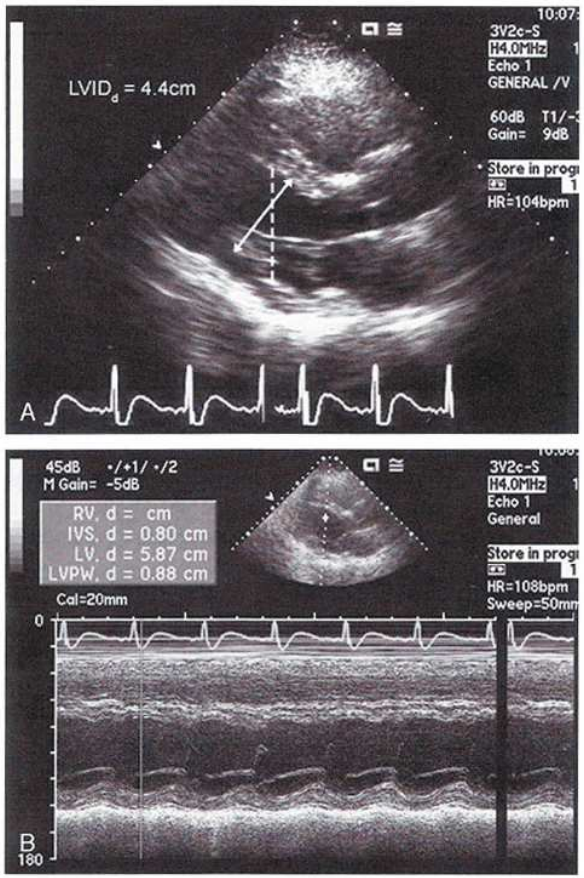


FIGURE 6.2. **Top:** A parasternal long-axis view recorded in diastole demonstrates the effect of cardiac angulation on M-mode measurements. Because the M-mode beam must conform to one of the two-dimensional interrogation lines, it frequently will intersect the left ventricle in a tangential manner (*dotted line*). This results in overestimation of the true minor-axis dimension, which in this example can be seen to be 4.4 cm (*solid arrow*). **Bottom:** The M-mode image from this view is presented and because of the tangential measurement has overestimated the internal dimension as 5.87 cm.

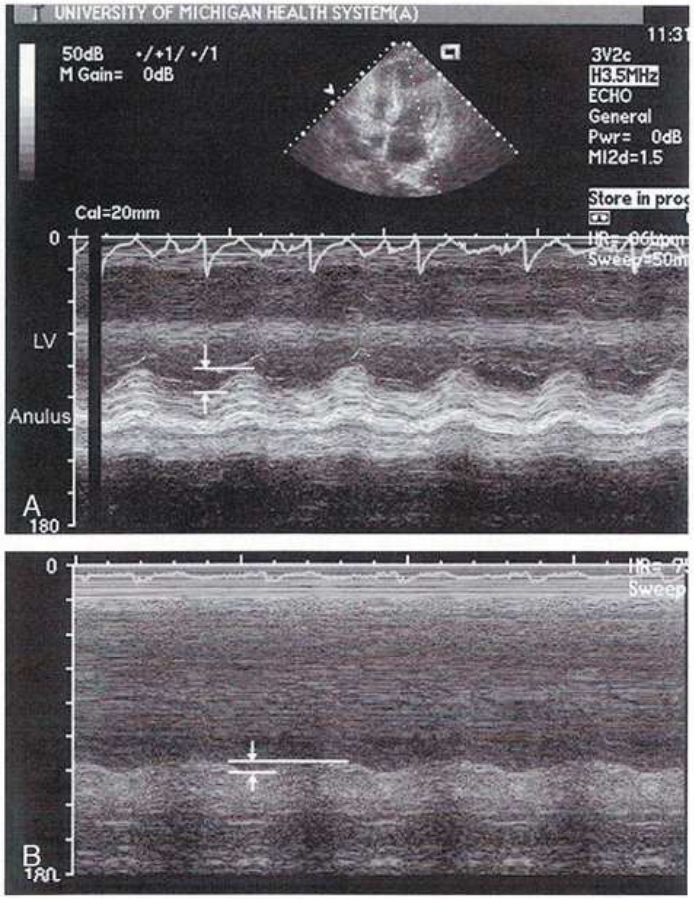


FIGURE 6.3. Apical view recorded in two patients demonstrates the measurement of the descent of the base with M-mode echocardiography. The M-mode interrogation beam has been directed from the apex of the heart through the lateral anulus. **Top:** Note the approximate 1 cm of anular motion toward the apex in systole. **Bottom:** Recording in a patient with severe systolic dysfunction reveals substantially decreased anular motion in systole.

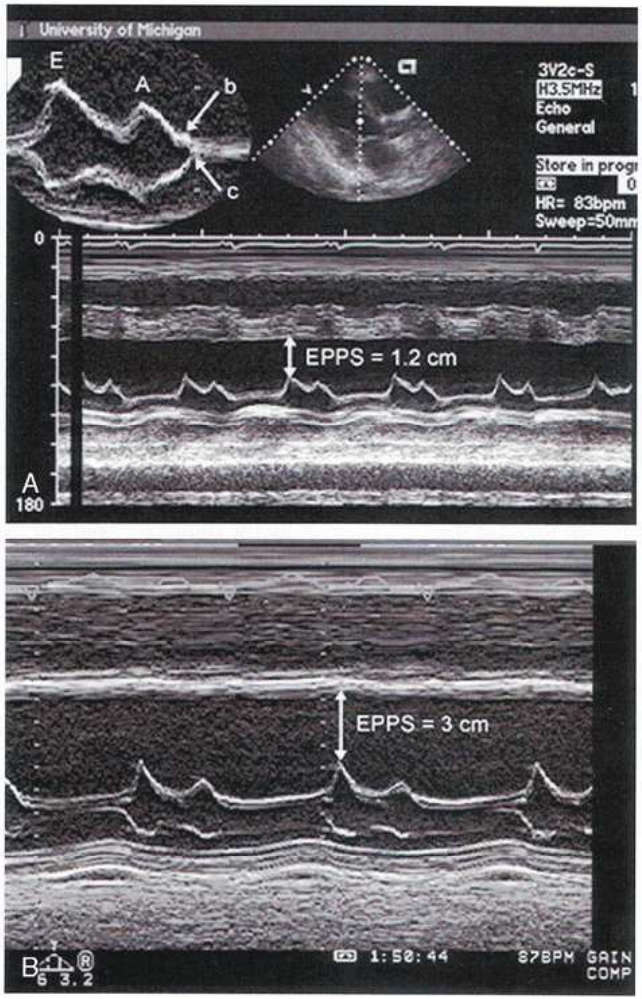


FIGURE 6.4. M-mode echocardiograms recorded in two patients with significant systolic dysfunction. **Top:** An E-point septal separation (EPSS) of 1.2 cm (normal, <6 mm). **Bottom:** Recording in a patient with more significant left ventricular systolic dysfunction in which the EPSS is 3.0 cm. Also note the interrupted closure of the mitral valve with a B bump **(top)**, indicating an increase in the left ventricular end-diastolic pressure.