A STUDY ON ELEVATED PULSE PRESSURE INDEX AS AN INDICATOR OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE AWARD OF THE DEGREE OF

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BRANCH – I M.D GENERAL MEDICINE

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MADURAI REG. NO : 201911112

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI, TAMILNADU, INDIA

MAY 2022

CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled "**A STUDY ON ELEVATED PULSE PRESSURE INDEX AS AN INDICATOR OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION**" is the bonafide work of **Dr.PRADEEP BALAJI.B** in partial fulfillment of the university regulations of The Tamil Nadu Dr. M.G.R. Medical University, Chennai, for M.D General Medicine Branch I Examination to be held in May 2022.

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This is to certify that the dissertation entitled "**A STUDY ON ELEVATED PULSE PRESSURE INDEX AS AN INDICATOR OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN TYPE 2 DIABETES MELLITUS**" is the bonafide work of **Dr.PRADEEP BALAJI.B**, to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of degree of Doctor Of Medicine (M.D) Branch-I - General Medicine, is a bonafide research work carried out by him under my direct supervision & guidance.

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DECLARATION

I,**Dr.PRADEEP BALAJI.B** solemnly declare that, this dissertation entitled "**A STUDY ON ELEVATED PULSE PRESSURE INDEX AS AN INDICATOR OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION**" is a bonafide record of work done by me at the Department of General Medicine, Government Rajaji Hospital, Madurai , under the guidance of Professor Dr A.SENTHAMARAI MD., Department of General Medicine, Madurai Medical college, Madurai from August 2021 to November 2021. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, Diploma to any other University, Board either in India or abroad. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Degree of Doctor of Medicine (M.D.), General Medicine Branch-I-examination to be held in May 2022.

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Study Title	:	Elevated pulse pressure index in Type 2 diabetes mellitus – an indicator of Left Ventricular Diastolic Dysfunction
Principal Investigator	:	Dr.B.Pradeep Balaji
Designation	:	PG in MD., General Medicine
Guide	:	Dr.A.Senthamarai, MD., (Gen.Med.) Professor of General Medicine
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The request for an approval from the Institutional Ethics Committee (IEC) was considered on the IEC meeting held on **11.08.2021** at GRH Auditorium, Govt. Rajaji Hospital, Madurai at 10.00 A.M

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This is to certify that this dissertation entitled **"A STUDY ON ELEVATED PULSE PRESSURE INDEX AS AN INDICATOR OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION"** of the candidate **Dr.PRADEEP BALAJI.B,** with **Registration Number 201911112** for the award of M.D degree in the branch of GENERAL MEDICINE. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file containing from introduction to conclusion pages and result shows 8% percentage of plagiarism in the dissertation.

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INTRODUCTION

Diabetes is among the most common chronic diseases in the world, affecting an estimated 6.4% of the global adult population. The increase in the incidence and prevalence of type 2 diabetes can be attributed to the increase in population age,obesity and physical inactivity.

The emergence of type 2 diabetes as a global pandemic is one of the major challenges in human health in the 21st century. Long considered a disease of the affluent western countries, type 2 DM has now spread to every corner of the world .Indeed there are now more people with diabetes residing in emerging economies than in industrialised nations.

Cardiovascular disease remains the main co-morbid condition and contributor to mortality in the setting of diabetes. This occurs most commonly in the form of coronary heart disease but also in the incremental risk associated with diabetes for cerebrovascular disease, peripheral vascular disease and heart failure.

Heart failure is a common, costly, disabling, and potentially deadly condition. Around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6–10% , the condition usually worsens with time. Heart failure is the leading cause of hospitalization in people older

than 65. Although some people survive many years, progressive disease is associated with an overall annual mortality rate of 10%.

Heart failure [HF] is classified in to

- HF with decreased ejection fraction
- HF with normal ejection fraction (DHF)

DHF has a prevalence of almost 50 % of total heart failure, and is increasing in incidence every year thus causing a high burden to the community and health care. Even though earlier studies showed better prognosis for DHF, recently concluded various studies have indicated morbidity and mortality similar to HF with decreased EF.

In addition to the traditional causes of DHF such as hypertension, aortic stenosis ,etc Diabetes as a cause of Diastolic dysfunction and hence to DHF has an increased recognition in recent years. Various studies has shown a prevalence of diastolic dysfunction to be 55 to 65 % among Diabetic individuals .

With the increasing incidence of diabetes, with increase in longevity, sedentary lifestyle and obesity, Diabetes will form a major cause of DHF, particularly, these individual risk factors most often co-exist. With this background presence of Diastolic dysfunction in diabetic patients was studied in our hospital.

AIM OF STUDY

To study the association between pulse pressure index and left ventricular diastolic dysfunction in type 2 diabetes mellitus and its usefulness as an indicator for the same in out patients at Govt Rajaji hospital and Madurai medical college.

REVIEW OF LITERATURE

DIABETES:

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Low levels of insulin to achieve adequate response and/or insulin resistance of target tissues, mainly skeletal muscles, adipose tissue, and to a lesser extent, liver, at the level of insulin receptors, signal transduction system, and/or effector enzymes or genes are responsible for these metabolic abnormalities.

The severity of symptoms is due to the type and duration of diabetes. Some of the diabetes patients are asymptomatic especially those with type 2 diabetes during the early years of the disease, others with marked hyperglycemia and especially in children with absolute insulin deficiency may suffer from polyuria, polydipsia, polyphagia, weight loss, and blurred vision.

CLASSIFICATION OF DIABETES

Diabetes can be classified into the following general categories:

1. Type 1 diabetes -due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood

2. Type 2 diabetes -due to a progressive loss of adequate β-cell insulin secretion frequently on the background of insulin resistance

3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)

4. Gestational diabetes mellitus -diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation

ADA Criteria for the diagnosis of diabetes

1. HbAIC >=6.5 % OR

2. Fasting plasma glucose >= 126 mg/dl . (Fasting is taken as no energy intake for 8 hours at least) OR

3. 2hour plasma glucose >=200 mg/dl in an OGTT. (to be done using a 75 g glucose load) OR

4. In a patient with classic symptoms of hyperglycemia, a random plasma glucose >= 200 mg

PREDIABETES

“Prediabetes” is the term used for individuals whose glucose levels do not meet the criteria for diabetes but are too high to be considered normal .Patients with prediabetes are defined by the presence of Impaired fasting glucose (IFG)

and/or Impaired glucose tolerance (IGT) and/or A1C 5.7–6.4% (39–47 mmol/mol)

Impaired glucose tolerance is defined as two-hour glucose levels of 140 to 199 mg per dL (7.8 to 11.0 mmol) on the 75-g oral glucose tolerance test,

Impaired fasting glucose is defined as glucose levels of 100 to 125 mg per dL (5.6 to 6.9 mmol per L) in fasting patients.Prediabetes should not be viewed as a clinical entity in its own right but rather as an increased risk for diabetes and cardiovascular disease (CVD). Criteria for testing for diabetes or prediabetes in asymptomatic adults is outlined in Prediabetes is associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension.

TYPE 2 DIABETES MELLITUS

Type 2 diabetes, previously referred to as “noninsulin-dependent diabetes” or “adult-onset diabetes,” accounts for 90–95% of all diabetes. This form encompasses individuals who have relative (rather than absolute) insulin deficiency and have peripheral insulin resistance.

The risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity. It occurs more frequently in women with prior gestational diabetes mellitus (GDM), with hypertension or dyslipidemia, with polycystic ovary syndrome, and in certain racial/ethnic subgroups (African American, American Indian, Hispanic/Latino, and Asian American). It is often associated with a strong genetic predisposition or family history in first-degree relatives (more so than type 1 diabetes). However, the genetics of type 2 diabetes is poorly understood and under intense investigation in this era of precision medicine

COMPLICATIONS

The long term complications from diabetes can be classified as

A)Microvascular or

B)Macrovascular.

there are other complications of diabetes that cannot be included in the two aforementioned categories such as dental disease, reduced resistance to infections, and birth complications among women with gestational diabetes

Microvascular complications include

1)Diabetic Neuropathy

2)Diabetic Nephropathy

3)Diabetic retinopathy

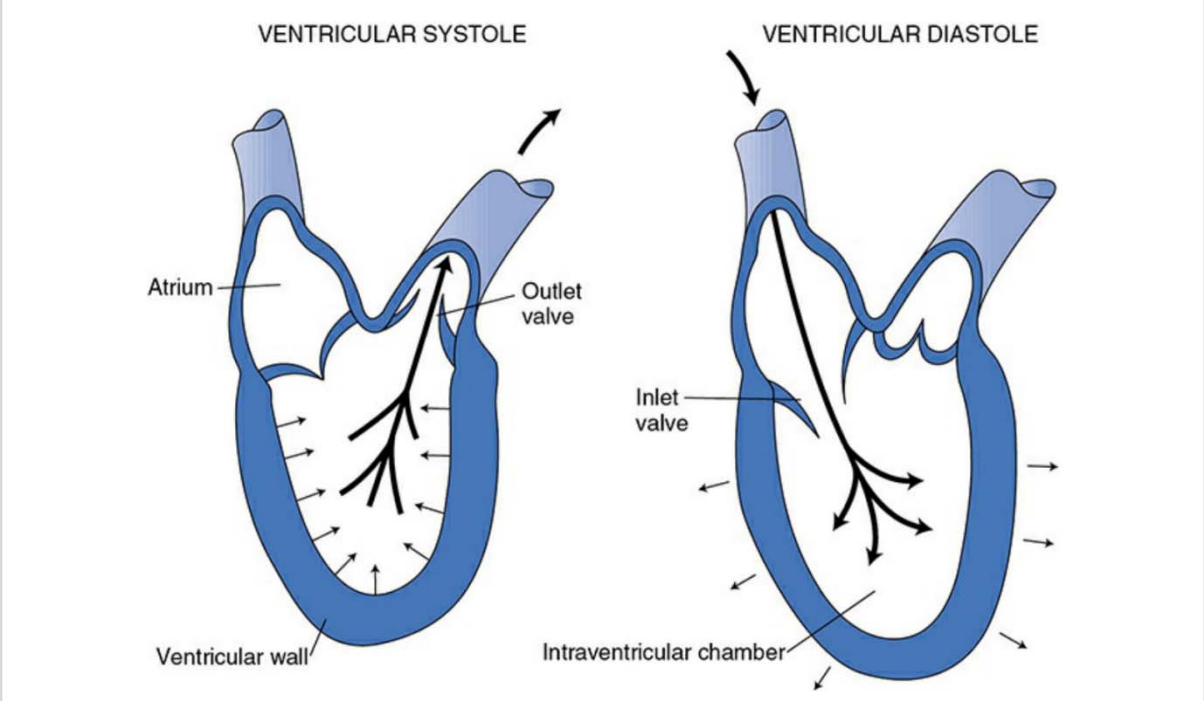
Macrovascular complications include cardiovascular disease, stroke, and peripheral vascular disease. Peripheral vascular disease may lead to bruises or injuries that do not heal, gangrene, and, ultimately, amputation.

SYSTOLE

This phase of the cardiac cycle during which the ventricular muscle cells are contracting is called systole. Because the pressure is higher in the ventricle than in the atrium during systole, the inlet or atrioventricular (AV) valve is closed.

DIASTOLE

When the ventricular muscle cells relax, the pressure in the ventricle falls below that in the atrium, the AV valve opens, and the ventricle refills with blood, as shown on the right side in Figure 1–5. This portion of the cardiac cycle is called diastole.



PHYSIOLOGY OF SYSTOLE

Ventricular systole begins when the action potential passes through the AV node and sweeps over the ventricular muscle—an event heralded by the QRS complex of the electro-cardiogram. Contraction of ventricular muscle cells causes intraventricular pressure to rise above that in the atrium. Because of the valve structure, the increased pressure behind the leaflets in the ventricle causes abrupt closure of the AV valve. Pressure in the left ventricle continues to rise sharply as ventricular contraction intensifies. When left ventricular pressure exceeds that in the aorta, the aortic valve passively opens.

The period between mitral valve closure and aortic valve opening is referred to as the isovolumic (or isovolumetric) contraction phase because during this

interval the ventricle is a closed chamber with a fixed volume. Ventricular ejection begins with the opening of the aortic valve.

In early ejection, blood enters the aorta rapidly and causes the pressure there to rise. Pressure builds up simultaneously in both the ventricle and the aorta as the ventricular muscle cells continue to contract in early systole. This interval is often called the rapid ejection period.

Left ventricular and aortic pressures ultimately reach a maximum called peak systolic pressure. At this point, the strength of ventricular muscle contraction begins to wane. Muscle shortening and ejection continue, but at a reduced rate. Aortic pressure begins to fall because blood is leaving the aorta and large arteries faster than blood is entering from the left ventricle. Eventually, the strength of the ventricular contraction diminishes to the point where intraventricular pressure falls below aortic pressure. Because of the aortic valve structure, the increased pressure behind the leaflets in the aorta causes abrupt closure of the aortic valve.

A dip, called the incisura or dicrotic notch, appears in the aortic pressure trace because a small volume of aortic blood must flow backward to fill the space behind the aortic valve leaflets as they close. After aortic valve closure, intraventricular pressure falls rapidly as the ventricular muscle relaxes. For a brief interval, called the isovolumetric relaxation phase, the mitral valve is also closed.

Ultimately, intraventricular pressure falls below atrial pressure, the AV valve opens, and a new cardiac cycle begins. Note that atrial pressure progressively rises during ventricular systole because blood continues to return to the heart and fill the atrium behind the closed AV valve..

The elevated atrial pressure at the end of systole promotes rapid ventricular filling once the AV valve opens to begin the next heart cycle. The ventricle has reached its minimum or end-systolic volume at the time of aortic valve closure. The amount of blood ejected from the ventricle during a single beat, the stroke volume, is equal to ventricular end-diastolic volume minus ventricular end-systolic volume. Note that under normal conditions, the heart ejects only about 60% of its end diastolic volume. The aorta distends or balloons out during systole because more blood enters the aorta than leaves .

The difference between diastolic and peak systolic pressures in the aorta is called the arterial pulse pressure. Typical values for systolic and diastolic pressures in the aorta are 120 and 80 mm Hg, respectively. At a normal resting heart rate of approximately 70 beats/min, the heart spends approximately two-thirds of the cardiac cycle in diastole and one-third in systole. When increases in the heart rate occur, both diastolic and systolic intervals become shorter. Action potential durations are shortened and conduction velocity is increased. Contraction and relaxation rates are also enhanced. This shortening of the systolic

interval tends to blunt the potential adverse effects of increases in the heart rate on diastolic filling time.

PHYSIOLOGY OF DIASTOLE

Diastole is the phase of the cardiac cycle that begins when the aortic valve closes and ends when the mitral valve closes, when LV pressure falls below aortic pressure.

A normal LV diastolic function can be clinically defined as the left ventricle's ability to receive an LV filling volume capable of ensuring an acceptable stroke volume while functioning at a low pressure regimen.

Diastole can be classified into four phases in simple words.

1. Isovolumetric relaxation is the time between the conclusion of LV systolic ejection (= aortic valve closure) and the opening of the mitral valve during which the LV pressure continues to fall rapidly while the LV volume remains constant.

This time is primarily related to active LV relaxation, with a smaller, variable contribution from constricted fibre elastic rebound.

2. LV quick filling, which occurs when the left atrial pressure drops below the LV pressure and the mitral valve opens. During this time, the blood accelerates to a maximum velocity, which is proportional to the magnitude of atrioventricular

pressure, and then ceases when the gradient ends. This ten-minute interval depicts a complex interaction between LV suction (= active relaxation) and the myocardium's visco-elastic characteristics (= compliance).

3. Diastasis, when left atrial and LV pressures are nearly equal and LV filling is essentially maintained by flow from pulmonary veins – with the left atrium acting as a passive conduit – with an amount varying with LV pressure, a

function of LV "compliance"; 4. Atrial systole, which corresponds to left atrial contraction and ends at mitral valve closure. LV compliance has a major impact

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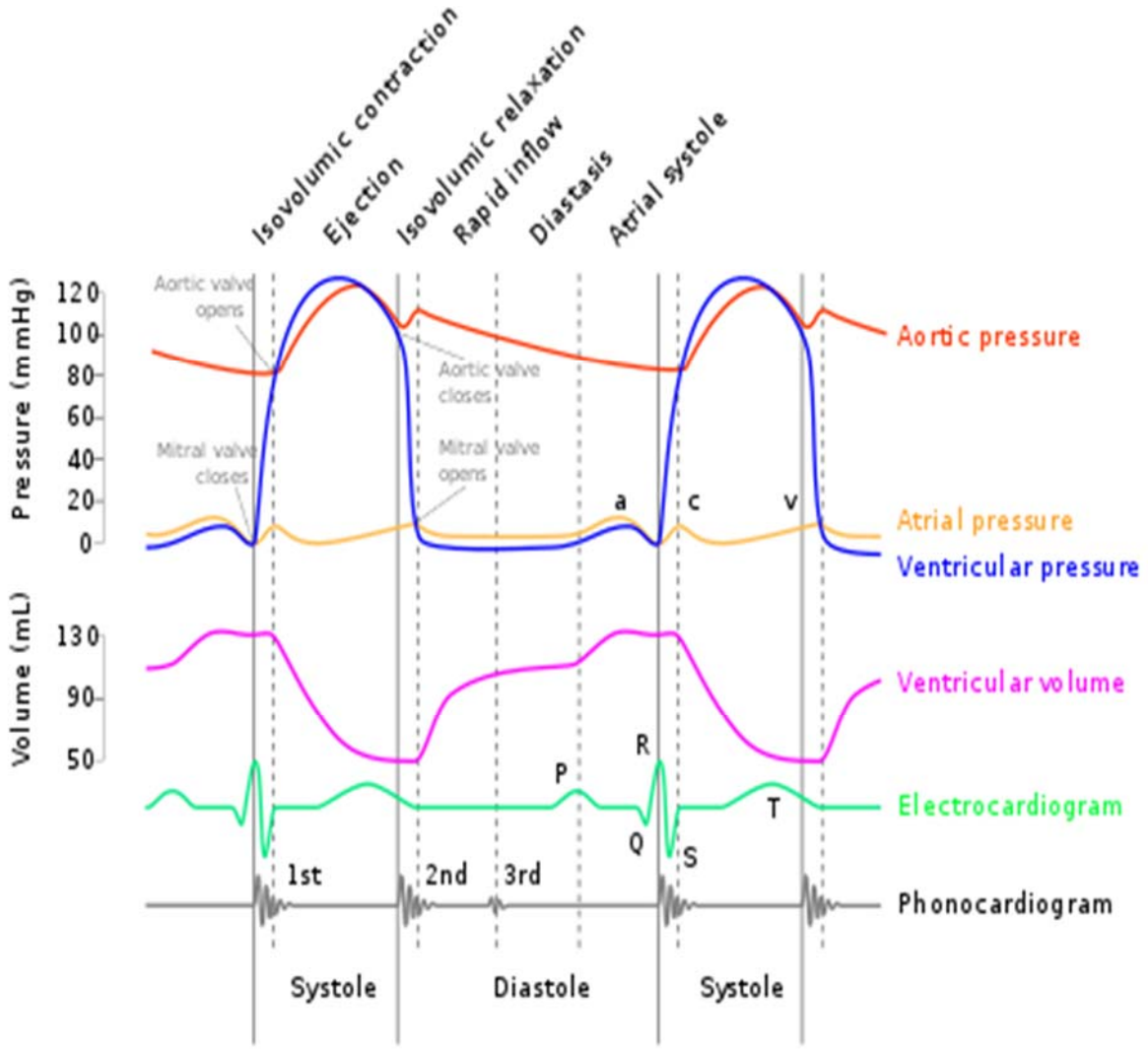
on this period.

Proper filling of the ventricles depends on 3 conditions: (1) the filling

pressure of blood returning to the heart and atria, (2) the ability of the AV valves to open fully (not be stenotic), and (3) the ability of the ventricular wall to expand passively with little resistance (i.e., to have high compliance). The healthy heart is very compliant during diastole so that filling normally occurs with only small increases in ventricular pressure.



The above figure shows cardiac cycle events occuring in the left ventricle

BLOOD PRESSURE

It is defined as the pressure exerted by the column of the blood over lateral wall of the vessel wall.

The blood pressure (BP) is not steady (unchanging) throughout the cardiac cycle but fluctuating, i.e. it is pulsatile. It rises and falls; reaching its maximum during systole of the heart, when it is called the systolic blood pressure (SBP); and falling to its minimum during diastole of the heart when it is called diastolic blood pressure (DBP)

$BP = CO \times TPR = (HR \times SV) \times TPR$

$SVR\ (TPR) = 80 \times (\text{mean arterial pressure} - \text{central venous pressure}) / CO$.

where *BP* is blood pressure,

SV is stroke volume,

TPR/ SVR is total peripheral resistance/Systemic Vascular Resistance

CO is cardiac output,and *HR* is heart rate.

As this study is about to find out the relationship between Pulse Pressure Index and Left ventricular diastolic Dysfunction , it is important to follow the recommendation as advised by the JNC 8

Measurement of Blood Pressure

Direct Method

The direct method of recording blood pressure (BP), in which an artery is punctured with a cannula connected to a manometer, was first used by Rev Stephen Hales, a British priest, in horses and dogs, in 1733. When he inserted a cannula into the femoral artery of a mare and connected it to a long glass tube, the blood rose to a height of 8 feet 3 inches. These days, direct method is used in research work in animals, and during cardiac and arterial catheterization in man.

Indirect Methods

Obviously, the direct method is not suitable as a routine clinical procedure. Indirect methods were, therefore, introduced; methods that are variations of a procedure called sphygmomanometry.

PRINCIPLE

A sufficient length of a single artery is selected in the arm (brachial artery), or in the thigh (femoral artery). The artery is first compressed by inflating a rubber bag (connected to a manometer) placed around the arm (or thigh) to stop the blood flow through the occluded section of the artery.

The pressure is then slowly released and the flow of blood through the obstructed segment of the artery is studied by

i. Feeling the pulse—the palpatory method.

ii. Observing the oscillations of the mercury column—the oscillometric method, and

iii. Listening to the sounds produced in the part of the artery just below the obstructed segment— the auscultatory method

A. Palpatory Method (Riva Rocci 1896)

1. Make the subject sit or lie supine and allow 5 minutes for mental and physical relaxation

2. Open the lid of the apparatus until you hear the “click”. Release the lock on the mercury reservoir and check that the mercury is at the zero level. If it is above zero, subtract the difference from the final reading. If it is below zero, add the required amount of mercury to bring it to zero level.

3. Place the cuff around the upper arm, with the center of the bag lying over the brachial artery, keeping its lower edge about 3 cm above the elbow. Wrap the cloth covering around the arm so as to cover the rubber bag completely, and to prevent it bulging out from under the wrapping on inflation. The cuff should neither be too tight nor very loose

4. Palpate the radial artery at the wrist and feel its pulsations with the tips of your fingers. Keeping your fingers on the pulse, hold the air bulb in the palm of your other hand and tighten the leak valve screw with your thumb and fingers. 5. Inflate

the cuff slowly until the pulsations disappear; note the reading then raise the pressure another 30–40 mm Hg.

6. Open the leak valve and control it so that the pressure gradually falls in steps of 2–3 mm. Note the reading when the pulse just reappears. The pressure at which the pulse is first felt is the systolic pressure. (It corresponds to the time when, at the peak of each systole, small amounts of blood start to flow through the compressed segment of the brachial artery). Deflate the bag quickly to bring the mercury to the zero level.

B. Oscillatory Method

Riva Rocci, in 1896 (i.e. before Korotkoff sounds were described) measured systolic pressure (SP) by the palpatory method while the diastolic pressure (DP) was recorded from the oscillations of the mercury column. As the cuff pressure was raised and then lowered, oscillations appeared which became maximum and then disappeared. Some workers took the midpoint of maximum oscillations as the DP while others considered the lower level of these oscillations as the DP (oscillations are best seen with an aneroid manometer). The students must have seen these oscillations in the mercury column. In a modification of the above method, a cuff is placed on the upper arm and a lightly-inflated one on the lower arm. As the pressure in the upper cuff is raised and lowered, pulsations can be recorded from the lower cuff

. 1. Digital Blood Pressure Monitor. It is a small, compact, battery-operated, palm-top unit with an LCD display screen and memory function. The recorder works on the 2-cuff “oscillometric measuring” principle described above, and automatically translates pulse wave oscillations into SP and DP. The advantage of this method is that it can be easily used by a layperson. The pressure measuring range is 0–280 mm Hg, while the HR range is 40–180/min. There are 2 input sockets, one on either side of the unit.

Connect the rubber bulb to one socket and the cuff (wrapped on the upper arm) to the other. The procedure is the same as that for auscultatory method except that you do not auscultate for Korotkoff sounds. As the pressure is raised and then lowered, the pressure and pulse readings appear on the screen and the final readings remain there until you switch off the unit.

C. Auscultatory Method (Korotkoff, 1905)

Before recording the BP by the auscultatory method, it should always be first recorded by the palpatory method so as to avoid missing the auscultatory gap.

Ordinarily no sound are heard when the chest-piece of a stethoscope is applied over the brachial (or any other) artery. However, if the cuff pressure is raised above the expected systolic pressure and then gradually lowered, a series of sounds, called Korotkoff sounds, are heard over the artery just below the cuff.

1. Place the cuff over the upper arm as described above, and record the BP by the palpatory method.

2. Locate the bifurcation of brachial artery (it divides into radial and ulnar branches) in the cubital space just medial to the tendon of the biceps which can be easily palpated in a semiflexed elbow as a thick, hard, elongated structure. Mark the point of arterial pulsation with a sketch pen

. 3. Place the chest-piece of the stethoscope on this point and keep it in position with your fingers and thumb of the left hand (if you are right-handed).

4. Inflate the cuff rapidly, by compressing and releasing the air pump alternately (sounds may be heard as the mercury column goes up). Raise the pressure to 40 to 50 mm Hg above the systolic level as determined by the palpatory method.

5. Lower the pressure gradually until a clear, sharp, tapping sound is heard. Continue to lower the pressure and try to note a change in the character of the sounds.

These sounds are called Korotkoff sounds and show the following phases: Phase I: This phase starts with a clear, sharp tap when a jet of blood is able to cross the previously obstructed artery

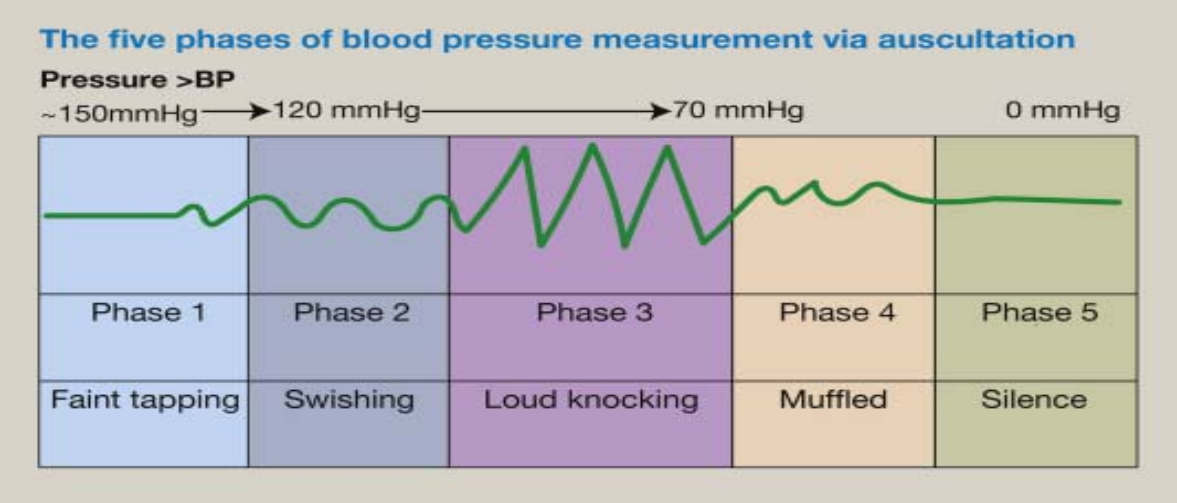
Note Criterion of systolic pressure The level at which the first sound (clear, sharp, or faint) is heard, is taken as the systolic pressure.

Phase II: The sounds become murmurish and remain so during the next 10–15 mm Hg fall in pressure when they again become clear and banging.

Phase III : It starts with clear, knocking, or banging sounds that continue for the next 12 to 14 mm Hg pressure, when they suddenly become muffled.

Phase IV :The transition from phase III to phase IV is usually very sudden. The sounds remain muffled, dull, faint and indistinct (as if coming from a distance) until they disappear. The muffling of sounds and their disappearance occurs nearly at the same time, there being a difference of 4–5 mm Hg (i.e. phase IV lasts for 4–5 mm Hg).

Phase V : This phase begins when the Korotkoff sounds disappear completely. If you reduce the pressure slowly, you will note that total silence continues right up to the zero level. 6. Take 3 readings with the auscultatory method and repeat 3 readings on the other arm.



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Recommendations

* Patient be rested in the seated position for at least 3 to 5 minutes prior to measuring BP.

* Neither examiner nor patient should talk during measurements.

* The patient's legs should be uncrossed and should be seated comfortably on a chair with arm rest and back support.

* Use the arm as the preferred site of BP measurement.

* Make sure the measuring device is adequately calibrated and maintained.

* Use a properly fitting cuff that fits the arm circumference . The bladder length at least should cover 80% of the arm circumference.

Recommended cuff sizes for adults are as follows:

❖ “Small adult” (12 × 22 cm): for arm circumferences between 22 and 26 cm

❖ “Adult” (16 × 30 cm): for arm circumferences between 27 and 34 cm

❖ “Large adult” (16 × 36 cm): for arm circumferences between 35 and 44 cm

❖ “Adult thigh” (16 × 42 cm): for arm circumferences between 45 and 52 cm

Cuff-based brachial BP is the most used method to measure BP, typically in the office setting. However, a rapidly growing body of evidence suggest that out-of-office BP methods, such as home BP monitoring and24-hour ambulatory BP monitoring (ABPM), are superior methods to evaluate BP. Mercury Sphygmomanometers are now not commonly available in clinical practice because of environmental concerns. Aneroid and electronic oscillometric manometers are accurate but periodically maintained by proper caliberation at every 12 months for their proper function.

Various Indices of Blood Pressure

Apart from Systolic and Diastolic Blood Pressure,

• Pulse Pressure(Systolic BP-Diastolic BP)

• Mean Arterial Pressure (Diastolic BP+ 1/3Systolic BP)

Pulse Pressure as a Tool for Prediction of Cardiovascular Events

Pulse pressure (PP) has been linked to an increased risk of coronary heart disease, stroke, and heart failure, especially in older people, according to current research. A high PP level is linked to a higher risk of myocardial infarction, congestive heart failure, and cardiovascular morbidity and mortality.

Problems with Pulse Pressure – as a tool

Because there is gradual amplification of the pressure wave from the aorta to the peripheral arteries, a characteristic that tends to decrease with age, the brachial pulse pressure index may not be a good predictor of central pulse pressure. Because the heightened emotional stress associated with a physical examination by a medical practitioner causes a greater increase in systolic BP than in diastolic BP, the clinical visit may result in an overestimation of normal pulse pressure values.Pulse pressure as an evaluation index, on the other hand, has two major drawbacks.

To begin with, Pulse Pressure varies from person to person. Blood pressure fluctuates a lot throughout a day, especially after using a short-acting antihypertensive medicine. Due to the considerable variability of blood pressure, adopting Pulse Pressure as an observation index is a bit of a gamble.

Second, Pulse Pressure is "floating," meaning it has no relationship to an absolute blood pressure level. A pulse pressure of 70 mm Hg, for example, may be coupled with a blood pressure of 180/110 mm Hg or 130/60 mm Hg. These Pulse Pressure restrictions are linked to blood vessel properties.

The difference between peak Systolic and end-Diastolic blood pressure (SBP–DBP) shows the pressure increase caused by ventricular contraction over and above the existing Diastolic blood pressure. Large-arterial stiffness (compliance) and wave reflection are the key factors of Pulse Pressure at any given heart rate and ventricular ejection %. Pulse Pressure is determined by vascular compliance for every given stroke volume. The ability of an artery to expand and recoil with each heart pulse and relaxation is measured by arterial compliance.

Vascular compliance can be broken down into two categories:

Intrinsic compliance and

dynamic compliance are two types of compliance.

When intravascular pressure is zero, intrinsic vascular compliance refers to the artery wall's basic compliance, which is linked to the arterial wall's composition. The intrinsic compliance of the artery wall varies depending on the biochemical features of the elastin–collagen mixture.

The elements that determine the artery wall's compliance are:

1. Elastin and collagen composition (structural determinants) and

2. the smooth muscle cells' vasoconstrictor tone (functional determinant)

Vascular dynamic compliance

The physical properties of the vascular tissue are reflected in vascular dynamic compliance. The ratio of the change in cross-sectional area of the artery divided by the change in pressure is defined as arterial compliance (dynamic compliance) in hemodynamics.

This value represents the geometry of the specimen as well as the softness (or stiffness) of the vessel. One of the most distinguishing characteristics of vascular tissue is that its elastic modulus is not constant, but rather a complex function of frequency that connects input pressure to volume stored. Vascular dynamic compliance fluctuates with blood pressure due to the alterability of the elastic modulus, which in turn causes the alterability of Pulse Pressure. The dynamic compliance of Pulse Pressure is linked to both its intrinsic and dynamic compliance.

Overcoming the problem with PP - Concept of Pulse Pressure Index(PPI)

Pulse Pressure has limitations as a measure for measuring cardiovascular outcomes because it is changeable and "floating." Yang et al introduced a new

metric, "pulse pressure/systolic pressure" termed "pulse pressure index (PPI)" for assessing cardiovascular outcomes in order to solve the shortcomings of Pulse Pressure.

They developed the following new equation for arterial compliance, systolic pressure, and PPI based on elastic chamber theory.

PPI = pulse pressure/systolic pressure = (Cs–Cd)/(Cs–C0),
(Cs - arterial compliance at systolic pressure and systolic pressure,

Cd - arterial compliance at diastolic pressure and,

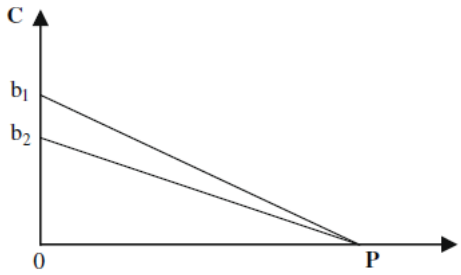
C0- arterial compliance at zero-pressure)

The renal resistive index (RI) is being calculated as (peak systolic velocity - minimum diastolic velocity)/peak systolic velocity, and it has been significantly associated with renal function. Pulse pressure index (PPI) is also derived from a formula similar to renal RI, i.e. (systolic blood pressure - diastolic blood pressure)/systolic blood pressure.

Advantages of PPI

It is clear that the value of PPI does not only depend on dynamic compliance (Cs–

Cd), but also on intrinsic compliance (C0). In situations even when the Pulse Pressure is the same or not, Pulse Pressure Index can reflect correctly vascular compliance, as long as intrinsic compliance is different. The value of PPI can overcome the ‘‘floating” limitation of PP.



(Relationship between blood pressure and arterial compliance. Dynamic compliance not only varies with blood pressure, but is also associated with intrinsic

compliance. C, dynamic compliance; b1 and b2, two different intrinsic compliance.)

Dynamic compliance is linked to both intrinsic and dynamic compliance, and it fluctuates with blood pressure. b1 and b2, two different intrinsic compliances; C, dynamic compliance. The "alterability" of PP is reduced when PPI increases.

Furthermore, it is obvious that the Pulse Pressure Index value is >0, a nondimensional value, and that it is also an absolute value with precise physics meaning.

PPI is a measure of vascular compliance that overcomes the floating effect. Pulse Pressure has both fixed and variable limits. The lower the vascular compliance, the lower the risk of cardiovascular disease. The closer the PPI

(Pulse Pressure Index) is to zero, the better. The closer the value is to zero, the higher the level of vascular compliance.

Pulse Pressure Index – Peculiar Properties

- PPI value is only between 0 and 1 ie >0 PPI<1
- PPI is An Absolute value
- PPI is A Non dimensional value
- PPI complies Physics

DIASTOLIC DYSFUNCTION

Diastolic heart failure (HFpEF)— Up to one-half of patients withheart failure have normal or near normal (i.e., “preserved”) ejection fraction (>50%). In these cases, the problem is not with the systolic pressure-developing processes but rather with the diastolic relaxation and passive distension processes. Diastolic dysfunction implies a stiffened heart during diastole such that increases in cardiac filling pressure do not produce normal increases in end-diastolic volume.

Some individuals (primarily elderly patients with hypertension and cardiac hypertrophy) who have some symptoms of cardiac failure (exertional dyspnea, fluid retention, pulmonary edema, and high end diastolic pressures) seem to have normal systolic function (ejection fractions >50%), and normal or even reduced ventricular end-diastolic volumes despite increased cardiac filling

pressure. Thus, the terms diastolic heart failure and heart failure with preserved systolic function have been used to describe this situation. This condition is associated with many common risk factors

- Hypertension,
- Atrial fibrillation,
- Diabetes or metabolic syndrome,
- Older age,
- Female sex,
- Inactivity,
- Renal dysfunction, and/or
- Obesity.

Most of the time, angiographic evaluation of the coronary circulation does not show significant large vessel disease. The symptoms mimic those of systolic heart failure (i.e., with reduced ejection fraction) (e.g., exertional dyspnea, fatigue, congestion, chest pain). Some degree of diastolic dysfunction is also commonly present in patients with reduced ejection fraction and may precede systolic problems. Potential causes of altered diastolic properties in heart failure include:

(1) decreased cardiac tissue passive compliance due to extracellular remodeling, collagen cross-linking, and other extracellular matrix protein alterations often associated with left ventricular hypertrophy resulting from hypertension,

(2) loss of myocardial elastic recoil that is partly responsible for early ventricular filling after systole,

(3) increased myofibrillar passive stiffness due to alterations in the myofibrillar giant protein titin,

(4) delayed myocyte relaxation early in diastole 238due to slow cytosolic calcium removal processes,

(5) inadequate adenosine triphosphate levels required to disconnect the myofilament cross-bridges rapidly, and

(6) residual, low-grade cross-bridge cycling during diastole due to calcium leaking from the sarcoplasmic reticulum. Metabolic comorbidities (diabetes, obesity) may trigger a systemic inflammatory state that leads to microvascular endothelial dysfunction allowing inflammatory cells to enter the myocardium. These trigger various paracrine signals that initiate various processes that lead to the passive compliance changes.

Ultrastructural features of diastolic dysfunction

The extracellular matrix (ECM), which corresponds to fibrillar collagen, is a crucial structure for both cardiac contraction and relaxation.

It allows the cardiomyocytes to be arranged in the most efficient way possible. proper allocation for force growth and shortening, resulting in a great assistance in maintaining optimal cardiac performanceMyocardial remodelling is accompanied with myocardial alterations. fibroblast proliferation, modification of the ECM are all examples of cell factors.There is an increase in interstitial and perivascular collagen, as well as a collagen network. The renin-angiotensin-aldosterone system promotes this significantly . As a result, to be considered a dynamic entity that plays a critical part in the adaptation of the myocardium to physiologic and pathologic stress . The ECM goes through a process. due to the balanced action of metalloproteases and proteolytic enzymes, there is a high rate of turnover.enzymes triggered by a variety of stimuli, including BNP and tissue inhibitorsmetalloprotease activity is being counterbalanced.

Thus, while collagen breakdown changes the geometry and function of contractile myocardium by upregulating metalloproteases, myocardial fibrosis emerges as a result of an imbalance in which collagen deposition outnumbers its degradation.

According to the ultrastructural view, two pathologic conditions can be hypothesised: the first, when collagen loss, such as after an acute myocardial infarction, deprives the myocardium of its essential support structure, resulting in a reduction in myocardial systolic function; the second, when the same collagen, the main component of myocardial fibrosis, determines both systolic and diastolic myocardial dysfunction In this context, not only the overall amount of collagen but also the distribution, configuration, disarray of collagen fibres (crosshatching), and the ratio of collagen type I to collagen type III play crucial roles in LV diastolic stiffness.

Clinical, hemodynamic and diagnostic aspects of diastolic dysfunction:

Clinical Aspects

In individuals with symptomatic HF, coexistence of systolic and diastolic dysfunction is highly common in the clinical context. In fact, LV stiffness (or compliance) is proportional to the length of myocardial fibres, which reflects LV end-diastolic dimensions. The influence of left atrial and capillary wedge pressures on LV diastolic performance also determines the development of symptoms in patients with LV systolic dysfunction. The clinical course of HF can take two divergent paths, parallel to the ultrastructural level. In the first, postinfarction LV dilation (= remodelling) causes systolic dysfunction and/or systolic heart failure, as it does after an acute myocardial infarction. In the second,

structural anomalies of the LV (= LV concentric geometry) cause DD functional changes. Diastolic heart failure increases when diastolic dysfunction becomes symptomatic - that is, when dyspnoea occurs. The majority of patients with isolated diastolic HF develop symptoms in response to stress rather than at rest (II NYHA class). Physical activity, as well as events such as anaemia, fever, tachycardia, and various systemic diseases, can cause or intensify symptoms. Because of the accumulation of pulmonary extravascular fluid, tachycardia lowers the time required for global LV filling, resulting in an increase in left atrial pressure and the appearance of dyspnoea.

The diagnosis of HF can be made with a simple clinical examination, however determining the diastolic aetiology necessitates an instrumental assessment. In reality, objective assessment of patients with diastolic HF might reveal the identical symptoms as those seen in systolic HF, and even a thoracic x-ray cannot distinguish the two conditions. Due to hypertension cardiomyopathy or other reasons, an ECG can reveal indications of LVH. Because DD is often asymptomatic, it is occasionally detected through a Doppler echocardiographic examination.

ECHO DOPPLER

The high practicality of transmitral Doppler indexes of diastolic function, which has been established in population studies to be acceptable and accurate for serial evaluations over time, adds to the diagnostic value of this instrument. To present, the evaluation of pulmonary venous flow [as well as innovative ultrasonic technologies such as tissue Doppler and colour M-mode derived flow propagation rate] have been shown to be effective in supporting standard Doppler indexes. The application of manoeuvres (Valsalva, leg lifting) to the Doppler transmitral pattern and/or different combinations of standard transmitral Doppler with the new tools (ratio between atrial reverse velocity duration and transmitral A velocity duration, ratio between transmitral E peak velocity and Tissue Doppler derived Em of the mitral annulus or flow propagation velocity [Vp]) are sufficient to predict capillary wedge pressure and to distinguish accurately variations.

\Some of these strategies are helpful even in specific scenarios such as sinus tachycardia and atrial fibrillation, whereas in the event of mitral valveprosthesis and aortic valve regurgitation, the pulmonary venous flow or the Valsalva manoeuvre applied to transmitral inflow must be favoured. Tissue Doppler can also "read" the percentage of cardiac fibrosis, which is the first step in DD. These techniques, when used alone or in combination, allow you to distinguish normal diastole as well as diagnose and track the course of DD from aberrant relaxation (grade I) to pseudo normal (grade II) and restrictive (grade III-IV) patterns.

Hemodynamics:

The pressure-volume loop expresses the distinctions between diastolic and systolic HF from a hemodynamic standpoint. Larger LV filling pressures correspond to increased LV volumes when systolic HF occurs, causing the loop to shift to the right. When diastolic HF occurs, the LV filling pressures rise in the presence of normal or even reduced LV volumes, causing the loop to move up and to the left. It is self-evident that diastolic and systolic dysfunction coexist in the later stages of HF.

Determinants of diastolic dysfunction:

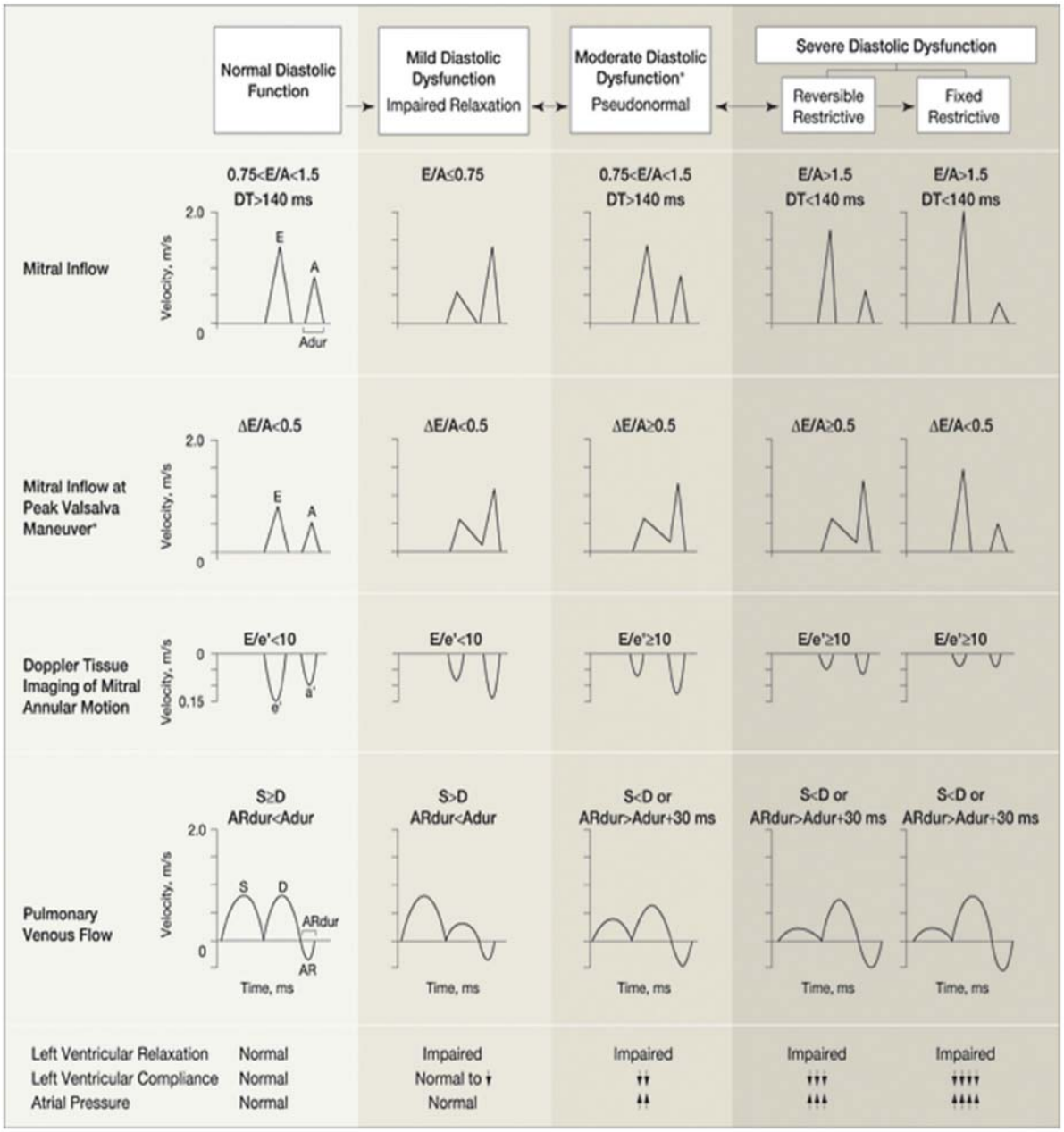
LV DD develops in a variety of cardiac diseases as well as extra-cardiac pathologies involving the heart (accumulation diseases such as amyloidosis, thyroid disorders, acromegaly, and others) and in myocardial ischemia due to coronary artery stenosis or even isolated coronary microcirculation dysfunction. Until date, arterial hypertension has been the primary cause of DD. Obesity and obesity, which frequently coincide with hypertension, have a significant impact on LV diastolic function, putting the left ventricle in a state of working overload. In this view, DD is one of the cardiac repercussions of the pluri-metabolic syndrome, in which arterial hypertension, obesity, glucose intolerance, and hypertriglyceridemia all coexist in the same person, with insulin resistance as their common matrix. Insulin resistance, which is typically seen in arterial

hypertension, is linked to a longer isovolumic relaxation period, which is independent of LV geometric alterations and greater afterload.

The change in diastolic isovolumic relaxation is most likely related to an increase in intracellular calcium, which has been found in insulin resistant hypertensives and is caused by an aberrant sarcoplasmic reticulum calcium re-uptake. LV diastolic function is also negatively affected by hormones produced by adipose tissue, such as leptin, which is involved in the control of body weight through food absorption and energy-giving cost. As observed in the Strong Heart Study cohort, the combination of arterial hypertension and diabetes mellitus decreases Doppler indicators of LV diastolic performance.

It's debatable if LV DD develops in tandem with LVH or emerges independently. True, DD is a direct result of pressure overload, with raised 24-hour blood pressure and, more importantly, an increase in nocturnal diastolic blood pressure. Recent research suggests that hypertension individuals' diastolic problems are linked to abnormally high levels of LV mass, which are disproportionate to the hemodynamic load anticipated by individual body size and cardiac load, rather than the LV mass values that usually describe LVH. In hypertensive individuals, abnormally large LV mass is a strong predictor of cardiovascular risk, even in the presence and absence of clear-cut LVH. The discovery that BNP levels rise gradually with the advancement of DD grading (from aberrant relaxation to restrictive Doppler patterns) in patients with diastolic

HF, regardless of the size of LV mass, supports the hypothesis of DD onset preceding the advent of LVH.



Clinical course and Prognosis of DHF :

Morbidity in Diastolic Heart Failure and Diastolic Dysfunction

\It is well recognised that diastolic heart failure is associated with a high rate of morbidity. In certain studies, the 1-year hospital readmission rate can reach 50%. Patients with diastolic heart failure are more likely to visit the doctor on a regular basis. As a result, the costs of diastolic heart failure are comparable to those of systolic heart failure. Approximately 18 percent of patients in the CHARMPreserved research were brought to the hospital for worsening heart failure after a mean follow-up interval of 3.5 years, with 4.2 percent having more than three admissions. Patients with diastolic heart failure are at risk for nonfatal myocardial infarction and stroke, according to a study by Gottdiener et al. Patients with isolated diastolic dysfunction, as opposed to overt diastolic heart failure, have been shown to have higher morbidity. Even investigations of asymptomatic, very young patients with confirmed normal coronary architecture imply that diastolic dysfunction is associated with greater morbidity.

Mortality in Diastolic Heart Failure and Diastolic Dysfunction:

Patients with diastolic heart failure have a mortality rate of 5% to 8% per year, compared to 10% to 15% in patients with systolic heart failure. According to Redfield et alresearch, .'s Isolated diastolic dysfunction, like diastolic heart failure, carries a higher mortality risk.

Recent research has also revealed that diastolic dysfunction has the same prognosis as systolic dysfunction.

Prognostic Indicators :

Clinical Predictors

1. New York Heart Association class : Higher the class more the mortality

2. Renal function : worsening renal function as determined by glomerular filtration rate affects prognosis

3. Age : age is a strong predictor of mortality in diastolic heart failure.] ¬

4.Brain Natriuretic Peptide The level of brain natriuretic peptide (BNP), which correlates with diastolic abnormalities as seen on echocardiogram,[89] has received some attention as a possible predictor of outcome.

5.Echo-Doppler

Diastolic heart failure is a common condition that is likely to become more common in the near future, given the high prevalence of hypertension, diabetes, and obesity, as well as the rising average age. Prospective cross-sectional and population-based research, particularly those incorporating echocardiography, are amassing data on prognosis. These findings are expected to improve clinical care for these patients by emphasising those who are at high risk of complications and death.

DIABETES AS A CAUSE OF DIASTOLIC DYSFUNCTION :

Ischemic cardiomyopathy and left ventricular (LV) dysfunction are the most frequent cardiovascular problems associated with diabetes. Diabetes is linked to heart failure, mostly due to its links to hypertension and coronary artery disease. However, evidence for the occurrence of myocardial dysfunction in diabetes patients without ischemic, valvular, or hypertensive heart disease has led to the proposal of a primary myocardial illness, "diabetic cardiomyopathy." Rubler et colleagues first hypothesised the existence of a diabetic cardiomyopathy in 1972 based on postmortem observations. In animal [98] and human research, impairments in both systolic and diastolic function in diabetes people have been documented. Diastolic dysfunction, which occurs before systolic damage, has been identified as an early indicator of diabetic heart muscle disease. The cause of this ventricular dysfunction is unknown, and there is some debate about it.

Diastolic irregularities have been proposed as an early functional impact of a particular diabetic cardiomyopathy in diabetic patients without diabetes sequelae or cardiovascular disease. Various problems in diastolic function, such as a prolonged isovolumic relaxation period, a delayed mitral valve opening and impairment in rapid diastolic filling, an increased atrial contribution to LV filling, and a lowered E/A mitral ratio, have all been seen. Abnormalities in LV diastolic function have been demonstrated in diabetic patients with normal systolic

function in the vast majority of studies. In asymptomatic, young type 1 diabetes patients, Raev et colleagues found a significant frequency of diastolic impairment with maintained systolic performance. Diastolic dysfunction appeared 8 years after diabetes beginning, while systolic dysfunction appeared considerably later, after 18 years of diabetes. The filling pattern has shifted from the early passive to the late atrially enhanced filling phase, according to these findings.

Surprisingly, the presence of the pseudonormal LV filling pattern, a more advanced stage of LV diastolic dysfunction, was not assessed in any previous Doppler studies until recently. Indeed, if preload reduction techniques (Valsalva manoeuvre, Glyceryl Trinitrate) or novel echo Doppler indices are not applied, diagnosis of a pseudonormal filling can be readily neglected. Using Valsalva manoeuvre and Glyceryl Trinitrate, a pseudonormal diastolic function was found in 17 to 28 percent of asymptomatic, normotensive type 2 diabetics in recent investigations. These research lead to the conclusion that LV diastolic dysfunction in this population may be far more widespread than previously thought.

Relation with glycemic control

Initial studies in diabetic rats demonstrated decreased cardiac contraction and relaxation, as well as biochemical abnormalities, which were restored with sufficient insulin therapy, with the degree of reversibility varying depending on the insulin dose.

Diastolic dysfunction and glycemic management in diabetic individuals are still a hot topic of discussion. The severity of diastolic dysfunction, as measured by computer assisted analysis of M-mode echocardiograms (time interval between minimal cavity dimension and mitral valve opening), was linked to the long-term quality of metabolic management in people with type 1 diabetes (mean value of HbA1c over the last two years).

Prospective investigations in type 2 diabetics have come to diverse conclusions, but a few studies have found a link between adequate glycemic management and improved diastolic dysfunction.

On the other hand, several studies found that even after a year of follow-up, improvements in glycemic management were not associated with changes in diastolic function.

Relation with severity of glycemic disturbance

Diastolic dysfunction has been linked to glucose homeostasis in a few modest investigations.

They found early signs of diastolic dysfunction (assessed by E/A mitral flow ratio) not only in patients with diabetes but also in those with impaired glucose tolerance, independent of the confounding role of ischemia, body weight, and blood pressure in a study of subjects with normal glucose tolerance, impaired glucose tolerance, and type 2 diabetes mellitus diagnosed by an oral glucose

tolerance test according to World Health Organization recommendations. They hypothesised that cardiac function is linked to glucose and HbA1c levels that are already below the diabetes threshold. The study's weakness is that it was conducted on a limited sample size.

Diastolic dysfunction and diabetes duration

Evidence of a change in LV diastolic function at an early stage of type 1 diabetes without correlation with specific complication, in which all patients were free of cardiovascular illnesses and had diabetes mellitus for less than 5 years, was found in older studies. However, M-mode echocardiography and phonomechanography were utilised to assess diastolic function, which was an unsatisfactory parameter.

Doppler echocardiography (E/A ratio) revealed similar results in newly diagnosed type 2 diabetes individuals who were free of microvascular problems and had no signs of hypertension or coronary artery disease. These findings of impaired diastolic function in patients with newly diagnosed diabetes or those who have had the disease for a short time and have had no microangiopathic complications suggest that this change may occur early in the course of type 2 diabetes and is unrelated to microvascular complications.

Pathogenesis :

Aside from animal studies, various human studies have looked into the relationship between diabetes and histopathological abnormalities. There have been reports of changes in intramyocardial coronary arteries, comparable to those seen in other organs of diabetes individuals. In some but not all individuals with or without overt congestive heart failure, endothelial proliferation and subendothelial hyaline thickening with PAS-positive material in the artery wall have been described. Diabetic hearts have also been found to have thickened capillary basement membranes and capillary microaneurysms. A small vessel disease was found in 72 percent of diabetic patients and just 12 percent of non diabetic subjects in a study conducted by Zoneraich et al in young normotensive type 1 diabetics.

Diabetic myocardium appears to be caused by reduced glucose tolerance.

Rather than increased synthesis, degradation is preferred. Interstitial anomalies may contribute to diastolic dysfunction by increasing end-diastolic stiffness and LV mass [99]. Interstitial changes appear to predominate for a period of time in less advanced forms of tissue abnormalities, and are accompanied with retained cell morphology consistent with normal systolic function. Collagen buildup in the extracellular matrix of the heart has been suggested as a possible diagnostic tool for diabetes patients' defective acoustic characteristics of the myocardium.

Diabetes and coronary microvascular dysfunction :

Myocardial cell injury and reactive fibrosis/hypertrophy can occur as a result of microvascular damage in the diabetic heart. Although focal microvascular changes did not appear to be adequate to explain widespread interstitial fibrosis, these findings focused on the anatomy of coronary microvessels rather than their dynamics. Transthoracic echocardiography, which visualises the distal left anterior descending artery and measures coronary flow reserve (CFR) as a hyperemic to resting velocities ratio, can now be used to assess coronary circulation function. The CFR has good feasibility and reproducibility, and it has excellent concordance with intracoronary Doppler flow wire-derived CFR. Impaired CFR shows coronary microvascular dysfunction when there is no epicardial coronary stenosis. In both type 1 and type 2 diabetes, a drop in CFR has been recorded, and it appears to be a direct result of high glycemia

Furthermore, aberrant CFR may be due to increased cardiac sympathetic activity. Diabetic patients are a group of people who are suffering from diabetes. An alternative explanation is insulin resistance, which alters CFR during a cold pressure test, a completely endothelium-dependent stimulus

The link between coronary microvascular and diastolic dysfunction in diabetes:

Diastolic dysfunction is visible in type 1 diabetic patients who do not have CAD and have CFR impairment. Uncomplicated hypertension, another illness characterised by poor coronary microcirculation, showed a similar association between the size of CFR reduction and the degree of myocardial DD. Because coronary flow occurs primarily during diastole, this link is unsurprising. Even in patients without CAD, a change in the time constant of LV isovolumic pressure fall, as determined by catheterization, is linked to lower coronary flow.

Hyperglycemia and insulin resistance, as well as sympathetic hyperactivity, endothelial dysfunction, and LV concentric remodelling, are all variables that contribute to the development of DD in people with diabetes. Diabetic patients should have a comprehensive transthoracic Doppler evaluation that includes diastolic function with tissue Doppler estimation of LVFP and coronary microvascular function with the CFR test.

Clinical significance of LV diastolic dysfunction in diabetes :

Heart failure, often known as congestive heart failure, is a serious public health issue. Despite having a normal LV ejection fraction, up to 50% of people in the community have heart failure due to diastolic dysfunction, according to several epidemiological studies. Diastolic irregularities may contribute to the

increased morbidity and mortality among diabetic patients, according to certain epidemiological and clinical evidence. Indeed, statistics from the Framingham Heart Study have demonstrated that diabetic people, regardless of coronary heart disease or hypertension, have a higher incidence of congestive heart failure in the community. It was also seen in people enrolled in myocardial infarction clinical trials. Patients with diabetes have more pronounced heart failure symptoms, require more diuretics, and have a worse prognosis than those without diabetes, despite having similar LV systolic performance. Diastolic dysfunction of the left ventricle is one possible cause for this disparity.

Diastolic dysfunction has lately been highlighted as having prognostic implications. Diastolic dysfunction, as diagnosed by comprehensive Doppler techniques, is frequent, often without accompanying cardiac heart failure, and is linked to significant increases in all-cause mortality. In a population-based sample of middle-aged and older persons, it has also been proven that a lower mitral E/A ratio is independently related with increased all-cause and cardiovascular mortality. It's worth noting that these predictive results included diabetes patients who were not subjected to any specific analysis. By the way, the prognostic significance of isolated diastolic dysfunction in diabetics is unknown at this time. The impact of isolated diastolic dysfunction in diabetes was solely studied in terms of exercise ability, not mortality.

Indeed, some investigations have shown that even in the absence of LV systolic failure, LV relaxation dysfunction might affect exercise tolerance.

LV diastolic dysfunction was supposed to influence maximal treadmill performance and explain lower maximal performance observed in patients with type 2 diabetes.

Treatment of DHF :

Acute Diastolic Heart Failure

The treatment for acute pulmonary oedema is quite similar to the treatment for systolic heart failure. It is life-saving to utilise oxygen, morphine, nitrates, and diuretics to treat venous congestion and hypoxia. Even at this acute stage, however, understanding that this could be diastolic heart failure rather than systolic heart failure would alter our treatment. We must be cautious of excessively forceful diuresis in individuals who fit the diastolic heart-failure profile of being elderly, diabetic, hypertensive, African, or Asian. Because the left ventricle has a steep pressure-volume curve, aggressive diuresis can result in severe hypotension. In addition, tachycardia is poorly tolerated in diastolic heart failure, and early administration of betablockers or calcium channel blockers is recommended in the presence of atrial fibrillation.

Long-Term Management :

Two large-scale randomised controlled studies, however, have lately offered some evidence for the therapy of diastolic heart failure.One of the more accurate surrogate endpoints for diastolic heart failure is left ventricular hypertrophy regression (LVH).

As a result, ACEI, angiotensin receptor blockers, diuretics, calcium antagonists, and aldosterone antagonists are helpful medications in the treatment of left ventricular hypertrophy.

Non-Drug Therapy :

It's critical to understand that losing weight, reducing salt intake, and exercising can all help with left ventricular hypertrophy regression.

Cardiac rehabilitation treatments are quite beneficial in the reconditioning of diastolic heart failure patients.

Diabetic management:

Long-term good glycemic control and prevention of microvascular consequences are the only proven treatments.

MATERIALS AND METHODS

PLACE OF STUDY :

This study was conducted in Govt. Rajaji hospital and medical college,Madurai

PERIOD OF STUDY :

From August 2021 to November 2021.

DESIGN :

An Observational Study. A total of 50 Diabetic patients were selected and

- Blood pressure measured from which pulse pressure was calculated.
- ECHO-Doppler study done.

METHODOLOGY :

SUBJECT SELECTION :

A. **INCLUSION CRITERIA** :

- Patient with DIAGNOSED TYPE 2 DIABETES MELLITUS
- Duration of DM > 5 YEARS
- Age below 50 years
- Patients not on any antihypertensive drugs

B. **EXCLUSION CRITERIA** :

- Systemic hypertension
- Valvular heart disease
- Restrictive cardiomyopathy
- Coronary artery disease
- Congestive heart failure
- Ejection fraction less than 50 %
- Poor echo window
- Patients not in sinus rhythm
- Diabetic macrovascular and microvascular complications

Ethics Statement :

The study protocol was approved by the institutional ethical committee of Madurai Medical College . Informed written consent was obtained from all the participants and all the clinical investigations were performed according to the principles which were expressed in the declaration of Helsinki. All patients gave consent to publication of their clinical data.

Assessment of BP:

All the BP measurements where are obtained only after echocardiography examination with the patient in supine position and after rest period of at least 15 minutes .The BP measuring instrument used was omron digital BP apparatus which uses oscillometric method for automatically measuring the BP. The BP was measured twice in each patient. Bilateral BP values were obtained in both arms and the higher value was used for analysis. Well controlled BP was defined as Systolic BP < 140 mmHg and Diastolic BP as < 90 mmHg and a poorly controlled BP was defined as systolic BP≥ 140 mmHg or diastolic BP>90 mmHg.

Echocardiographic Assessment:

All echocardiography evaluations were performed by a single trained and experienced cardiologist using transthoracic echocardiography. All the participants were breathing quietly and in classical left lateral position during echo assessment. Two dimensionally guided M mode images and Two dimensional images were recorded initially. At the tips of mitral leaflets probe was placed to get the left ventricular inflow pattern and waveforms in apical four chamber view. Pulsed tissue Doppler image (TDI)was obtained with the probe placed at septal and lateral corners of the mitral valve annulus in apical four chamber view. The study defined LVDD as an E to transmitral A wave velocity

(A) ratio of ≥0.9, or E/Ea (E/e')≥15. Left ventricular ejection fraction is measured using the modified Simpson method.

Definition of Diabetes mellitus :

Patients were considered to be Diabetic if,

- Individuals who are already on OHA'S or Insulin

(or)

- Symptoms of Diabetic mellitus and Random blood sugar > 200mg/dl

(or)

- Fasting Plasma Glucose > 126 mg/dl

(or)

- Two hour Plasma Glucose > 200 mg/dl during an OGTT.

Laboratory investigation:

Samples for

- Blood Urea , Serum Creatinine,
- Random Blood Sugar
- Urine Albumin, Urine Sugar,
- Urine Protein ,
- Complete Blood Count were collected.
- 12 lead Electrocardiogram was obtained in all patient

Statistical analysis

Statistical analysis were performed with IBM SPSS version 26 (SPSS Inc., Chicago, IL). Descriptive statistics was computed. Data were tested for normality using Shapiro wilks normality test. Due to the skewed data levels, mann whitney U test was used for between group analysis. Kruskal wallis test was used to analyse between cholesterol levels and PPI. Chi square test was used to analyse categorical variables. Spearman rank correlation test was used to analyse between cholesterol and PPI. Receiver Operating Characteristic Curve was used to find out cut-off point of marker (PPI) in predicting LVDD. A significance was set as $p < 0.05$.

Table 1 Baseline characteristics of the study population

	Minimum	Maximum	Mean	Std. Deviation
Age	29	39	35.96	2.73
Systolic Bp	100	140	121.14	10.83
Diastolic Bp	60	90	75.59	10.07
Pulse Pressure	30	70	45.59	10.54
Pulse Pressure Index	0.25	0.54	0.37	0.07
RBS	78	160	122.24	19.59
Cholesterol	108	230	155.90	27.54
LVEF	54	70	59.60	4.06
E/A	0.66	1.7	0.91	0.26
E/e'	10	24	15.02	2.90

		LVDD				
			LVDD -ve		LVDD +ve	
SEX	Male	28	80.00%	7	46.70%	0.04*
	Female	7	20.00%	8	53.30%	

Fischer exact test; * ($p<0.05$)

Table 2: Descriptive analysis of gender in study population (N=50)

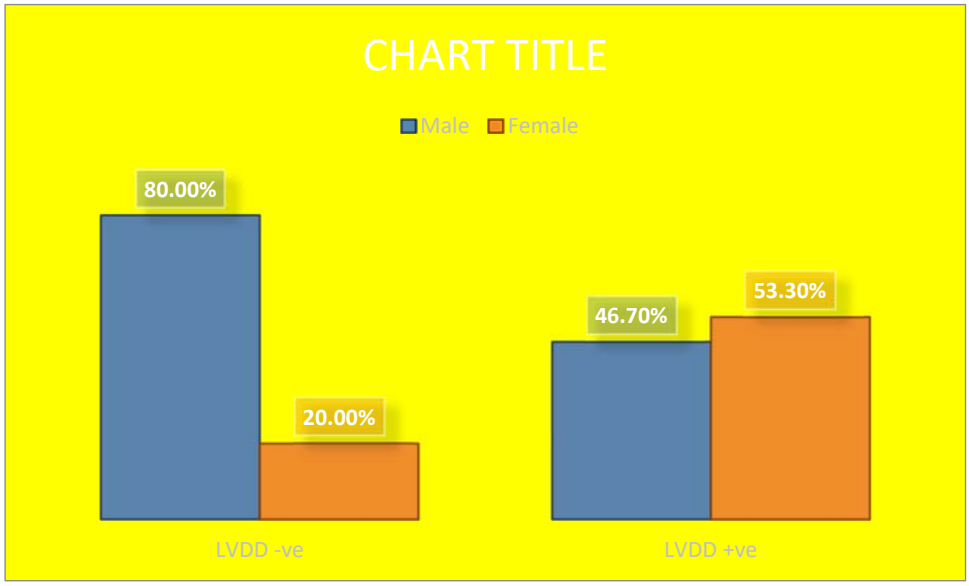


Figure 1: Bar chart of gender distribution in LVDD+VE and LVDD -ve groups

	LVDD	Mean	SD	p value
Age	-ve	36.0	2.7	0.798
	+ ve	35.8	2.9	
Systolic Bp	-ve	119.9	11.1	0.258
	+ ve	123.9	10.0	
Diastolic Bp	-ve	79.3	9.3	0.001*
	+ ve	67.2	6.0	
Pulse Pressure	-ve	40.7	7.5	0.001*
	+ ve	56.8	7.3	
Pulse Pressure Index	-ve	0.3	0.1	0.001*
	+ ve	0.5	0.0	
RBS	-ve	119.9	19.0	0.231
	+ ve	127.6	20.5	
cholesterol	-ve	142.1	18.2	0.001*
	+ ve	188.2	16.0	
LVEF	-ve	59.6	4.1	0.839
	+ ve	59.7	4.1	
E/A	-ve	0.8	0.1	0.001*
	+ ve	1.2	0.2	
E/e'	-ve	13.5	1.0	0.001*
	+ ve	18.6	2.6	

mann whitney U test; * ($p<0.05$)

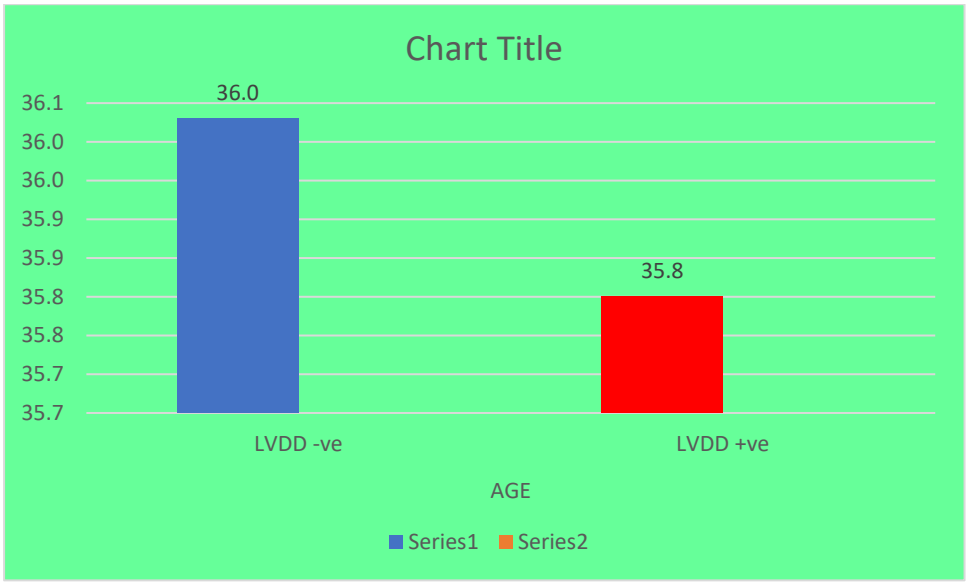


Figure 2: Bar chart distribution of AGE in LVDD+VE and LVDD -ve groups

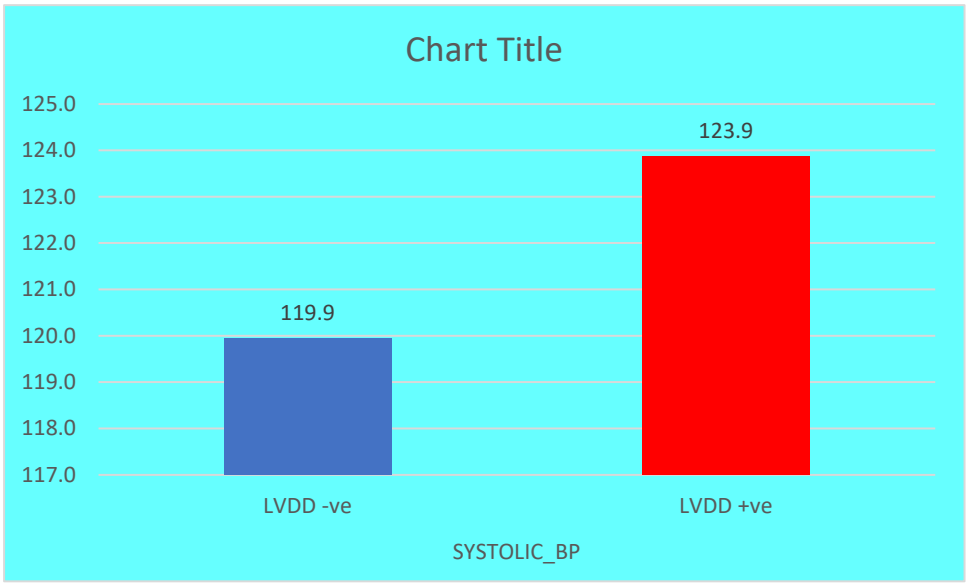


Figure 3: Bar chart distribution of SYSTOLIC BLOOD PRESSURE in LVDD+VE and LVDD -ve groups

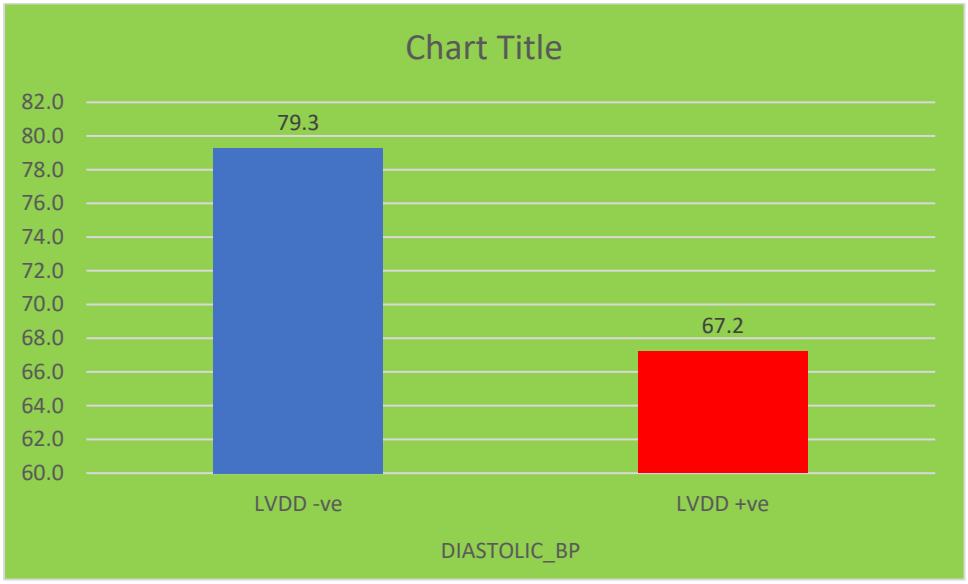


Figure 4: Bar chart distribution of DIASTOLIC BLOOD PRESSURE in LVDD+VE and LVDD -ve groups

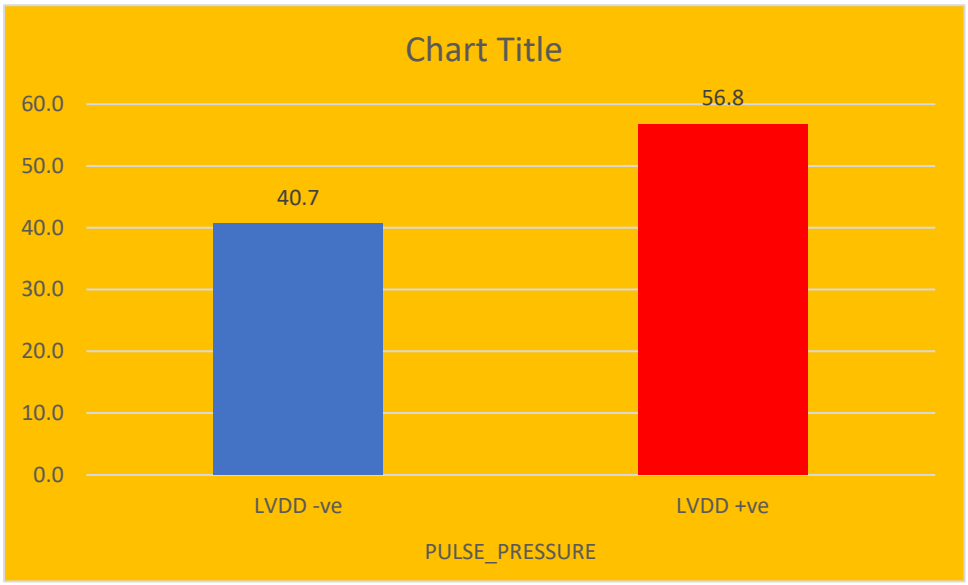


Figure 5: Bar chart distribution of pulse pressure in LVDD+VE and LVDD -ve groups

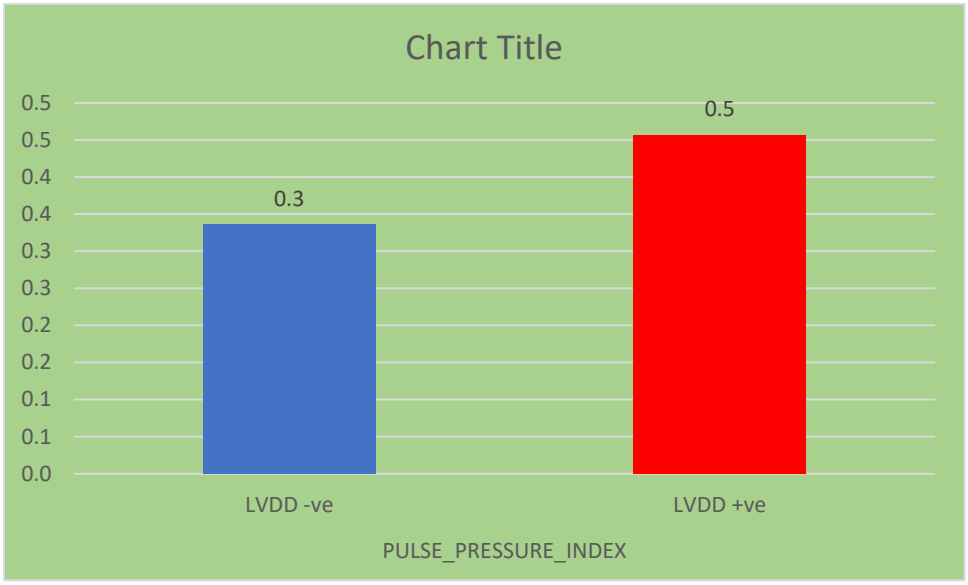


Figure 6: Bar chart distribution of PULSE PRESSURE INDEX in LVDD+VE and LVDD -ve groups

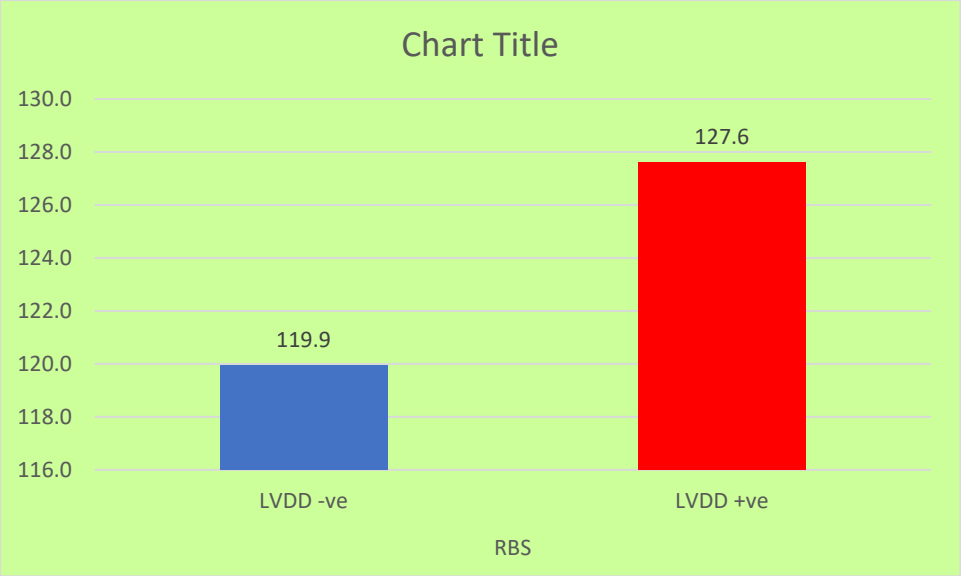


Figure 7: Bar chart distribution of RANDOM BLOOD SUGAR in LVDD+VE and LVDD -ve groups

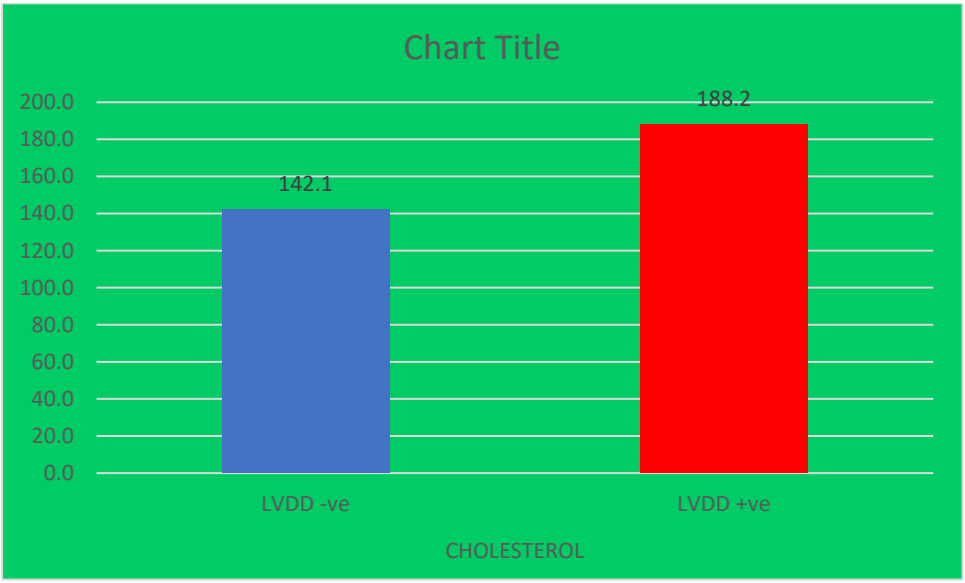


Figure 8: Bar chart distribution of SERUM CHOLESTEROL in LVDD+VE and LVDD -ve groups

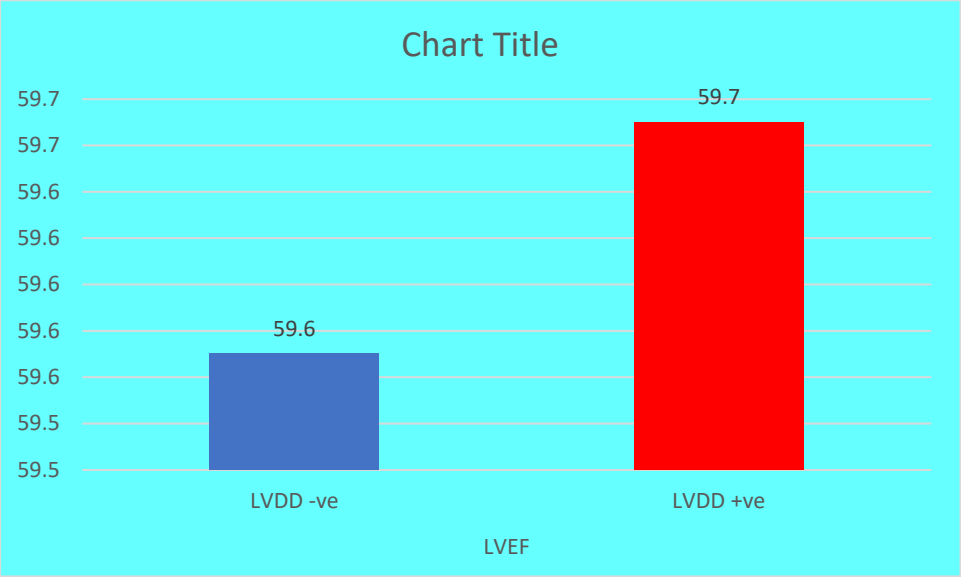


Figure 9: Bar chart distribution of LV EJECTION FRACTION in LVDD+VE and LVDD -ve groups

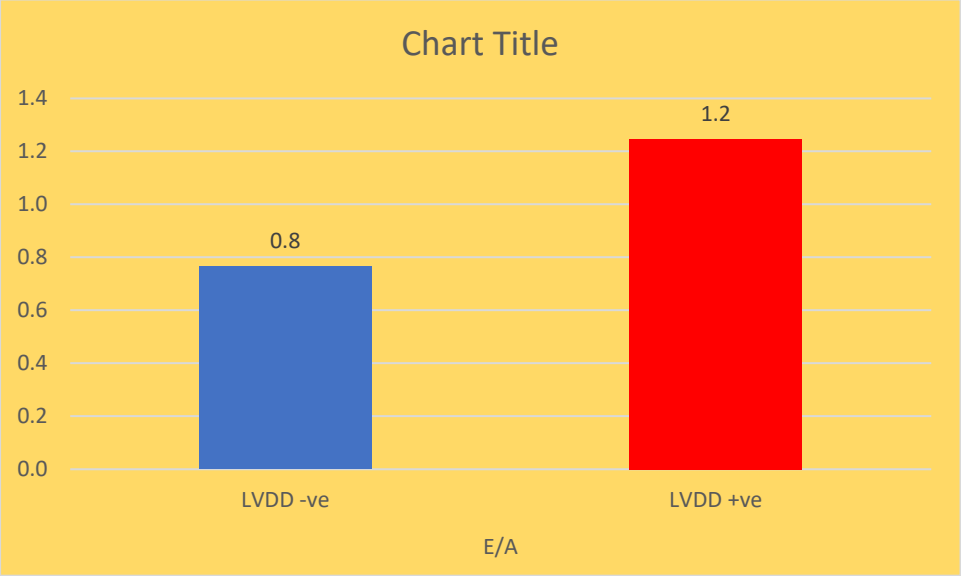


Figure 10: Bar chart distribution of E/A in LVDD+VE and LVDD -ve groups

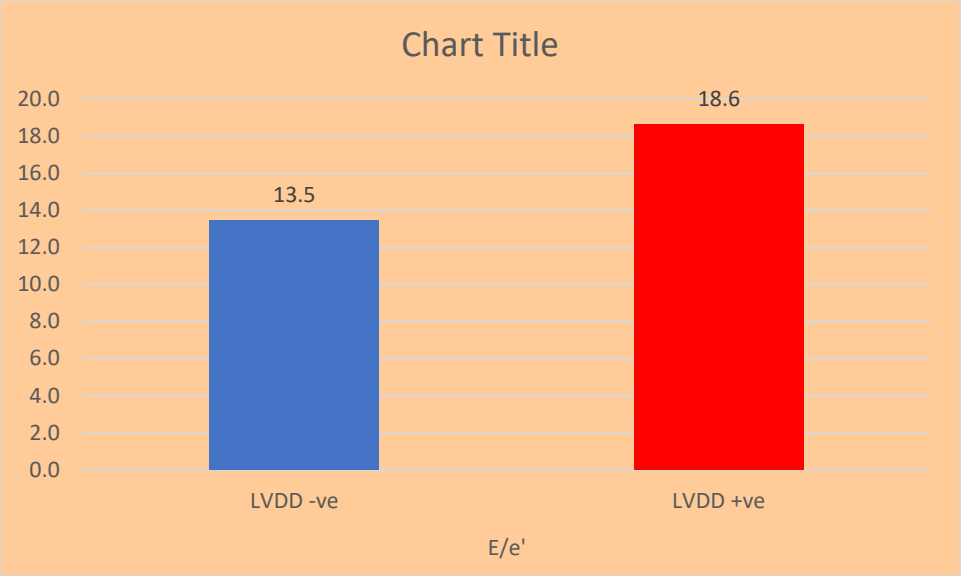


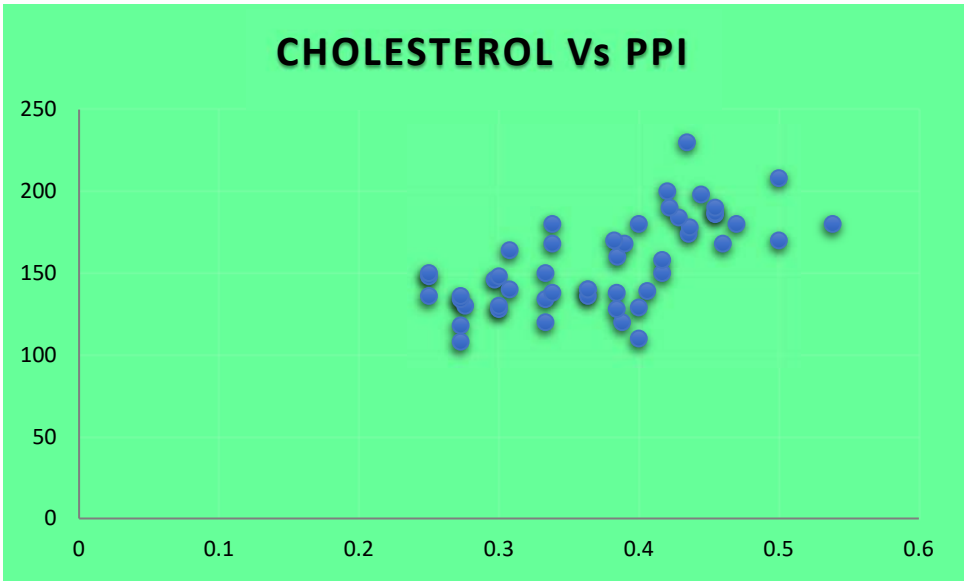
Figure 11: Bar chart distribution of E/e' in LVDD+VE and LVDD -ve groups

Correlations

			CHOLESTEROL
PULSE PRESSURE INDEX	Pearson Correlation (r value)	1	.646**
	P value		.000
	N	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

Relationship of PPI and LVDD among diabetic patients shows positive correlation (r=0.646) which was statistically significant (p<0.001)

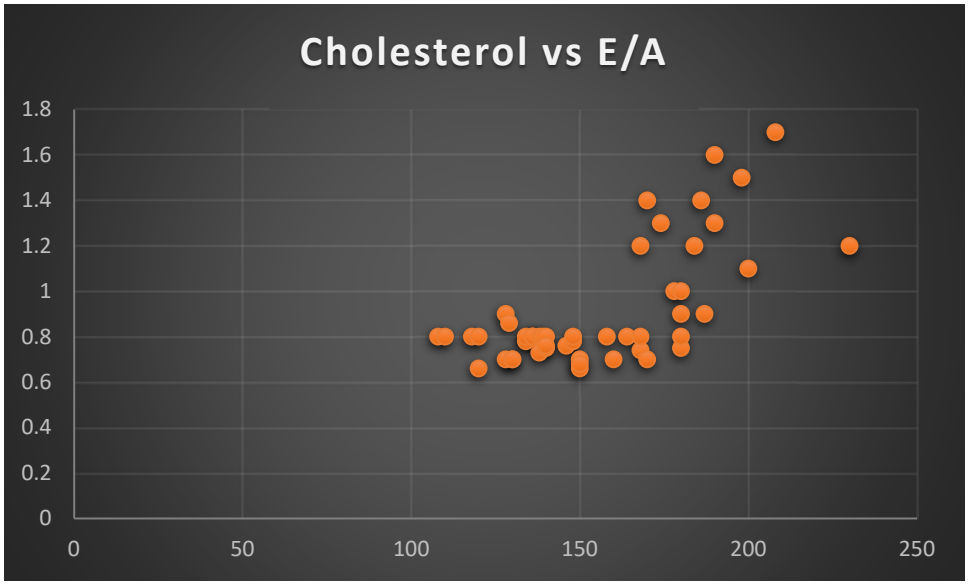


Correlations

			E/A
cholesterol	Pearson Correlation (r value)	1.000	0.536**
	P value	.	.001
	N	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

Relationship of E/A and LVDD among diabetic patients shows positive correlation (r=0.536) which was statistically significant (p<0.001)

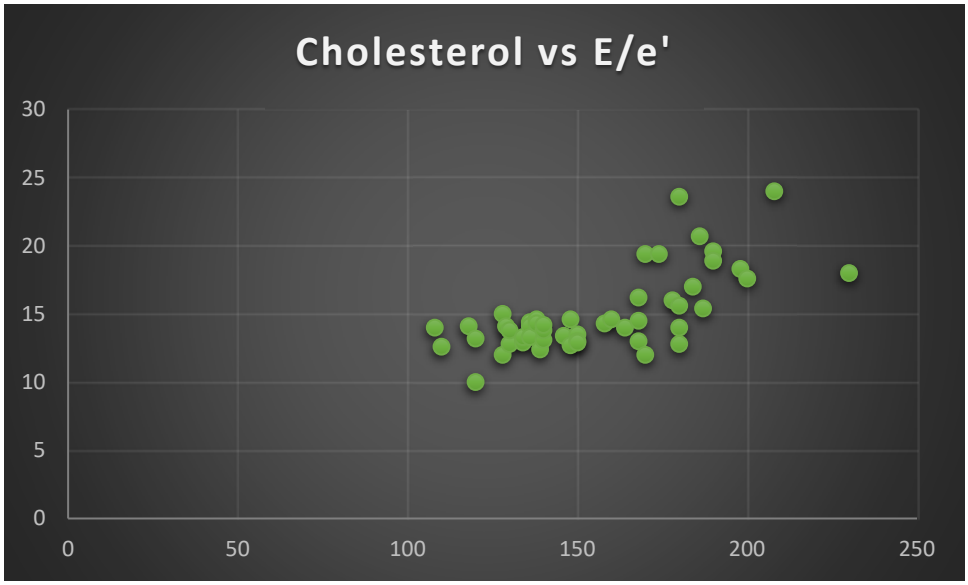


Correlations

			E/e'
cholesterol	Pearson Correlation (r value)	1.000	.626**
	P value	.	.001
	N	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

Relationship of E/e' and LVDD among diabetic patients shows positive correlation (r=0.626) which was statistically significant (p<0.001)

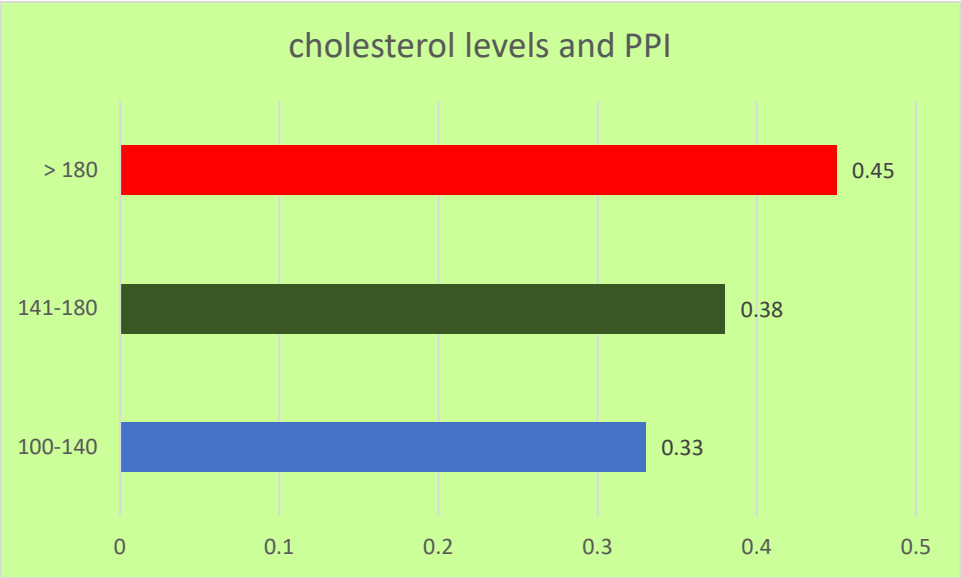


Cholesterol levels	N	Mean	Std. Deviation	p value
100-140	21.00	0.33	0.05	
141-180	20.00	0.38	0.08	0.001*
> 180	9.00	0.45	0.02	

Kruskal wallis test ;*. ($p<0.05$)

Pairwise Comparisons of cholesterol groups					
Sample 1-Sample 2	Test Statistic	Std. Error	Std. Test Statistic	P value	Adj. p value
> 180-141-180	9.972	5.659	1.762	.078	.234
> 180-100-140	13.847	5.659	2.447	.014	.043*
141-180-100-140	3.875	4.458	.869	.385	1.000

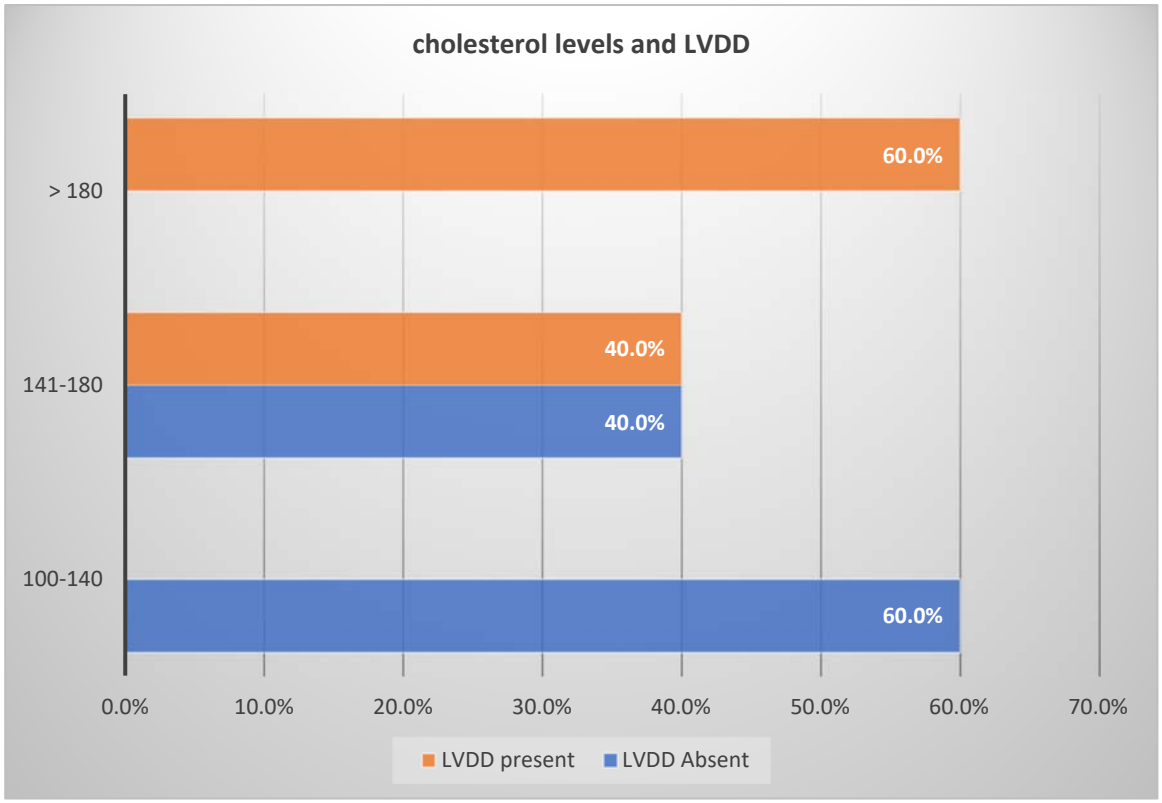
Post hoc Dunn bonferroni test; *. ($p<0.05$)

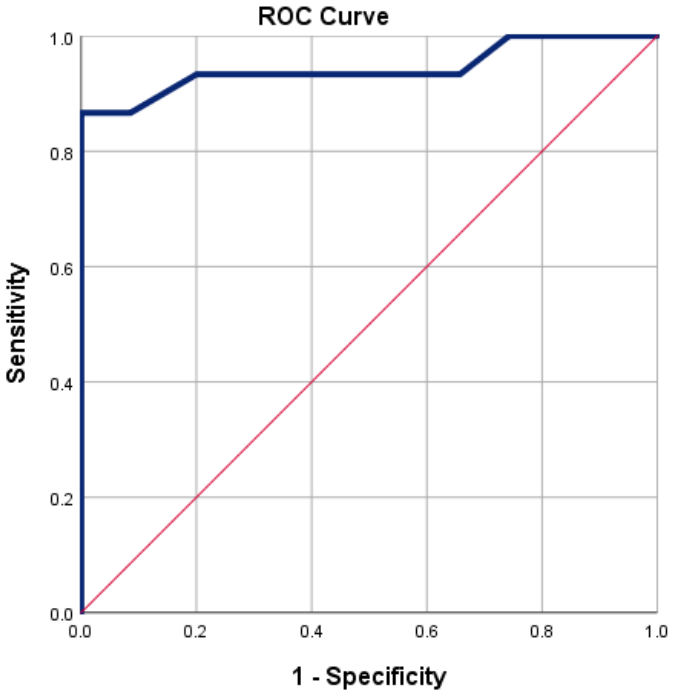


Pulse pressure index in various cholesterol groups

	LVDD -ve		LVDD + ve		
100-140	21	60.0%	0		
141-180	14	40.0%	6	40.0%	0.001*
> 180	0		9	60.0%	

Chi square test; * ($p<0.05$)


cholesterol levels and LVDD
> 180
141-180
100-140
60.0%
40.0%
40.0%
60.0%
0.0%
10.0%
20.0%
30.0%
40.0%
50.0%
60.0%
70.0%
LVDD present
LVDD Absent



Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PPI	0.944	0.046	0.001*	0.853	1.000

ROC curve for early prediction of markers for LVDD

Predictor marker	Cut Off value	Sensitivity (%)	Specificity (%)
PPI	≥0.373	93	66

PPI equal to or greater than 0.373 was considered as a predictor factor for LVDD in diabetic cases (P<0.001) with sensitivity of 93 and specificity of 66, and area under the ROC curve (AUC) of 0.944.**

DISCUSSION

This Study was done in a total of 50 type 2 diabetes mellitus patients.

- Of the total 50 populations males were 35 and females were 15.
- The study population's mean pulse pressure index was 0.3 in LVDD-ve cases and 0.5 in LVDD+ve cases.
- This Study showed that the mean age of diastolic dysfunction is less than the mean age of diabetic patients not having diastolic dysfunction that is age of patients not having diastolic dysfunction was 36 whereas mean age of patients having diastolic dysfunction was 35.8 but this does not have a significant p value.

Gender and Study

Patients are categorized under gender and their characteristics regarding diastolic dysfunction was compared.

• Of the 35 males in the study population, 7 patients had left ventricular diastolic dysfunction and 28 did not.

• Of the 15 females in the study population, 8 patients had left ventricular diastolic dysfunction.

This study revealed that Left Ventricular Diastolic Dysfunction is common in Females.

Systolic and Diastolic BP in the Study and LVDD

Systolic BP of the study population was compared between patient having left ventricular diastolic dysfunction and not.

This study revealed that Elevated systolic BP is common in patients with left ventricular diastolic dysfunction.

Diastolic BP was compared in the study population with presence or absence of diastolic dysfunction.

This study revealed that Diastolic Blood Pressure is decreased in the patients having left ventricular diastolic dysfunction.

Pulse Pressure in the Study Population and LVDD

Pulse pressure was compared in study population between patients having

diastolic dysfunction and its absence.

This Study revealed that

•Pulse Pressure is elevated in patients having left ventricular diastolic dysfunction and

• Pulse Pressure is less in patients having no left ventricular diastolic dysfunction.

Pulse Pressure Index and Left Ventricular Diastolic Dysfunction

Pulse pressure index was compared between patients having left ventricular diastolic dysfunction and its absence.

This study found that

• Pulse Pressure Index is elevated in patients with left ventricular diastolic dysfunction.

• Patients with less pulse pressure index had no diastolic dysfunction.

This also correlates with previous studies.

Relationship of pulsepressure index and left ventricular diastolic dysfunction among diabetic patients shows a positive correlation($r=0.646$) which was statistically significant ($p<0.001$).

CONCLUSION

This study clearly establishes that there is a definite and linear relationship between Pulse Pressure Index (PPI) and Left Ventricular Diastolic

Dysfunction(LVDD) in diabetic patients . The relation was analyzed using multivariate analysis . It showed that Pulse Pressure Index has an odds ratio of 1.027 and P value of <0.001 which is statistically significant.

This study concludes that Pulse Pressure Index and Left Ventricular Diastolic Dysfunction are directly related in patients with Type 2 Diabetes Mellitus and is therefore an useful predictor of Left Ventricular Diastolic Dysfunction.

LIMITATIONS OF THE STUDY-PPI & LVDD

Limitation regarding PPI

Pulse Pressure Index is a new concept and it is nascent.

That too the study population of the above was small.

No large general population studies have been conducted so far and poor literature support.

Limitation regarding LVDD

In 2016, American Heart Association concluded that No Single Parameter to be used for assessing Diastolic Dysfunction.

It should follow an algorithm of measuring 4 necessary parameters. They are

* Left Atrial Pressure ,(Normal/ Elevated)

*E/A,E to A wave ratio (<0.8/>0.8)

* Deceleration Time (< 200 ms />200 ms)and

* E/e'(Average septal E/e'<14/>14).

AHA(American Heart Association) recommends to measure all the 4 parameters and to diagnose LVDD only when 2 or more of the above 4 parameters are met. In this study only E/e'(E/Ea) is used.

PROFORMA

Name

Diabetic OP number

Age

Occupation

Sex

Personal Data

1. Smoking

2. Alcohol

3. Life style

4. Duration of DM

on OHA's or on Insulin

5. Systemic hypertension

6. Dyslipidemia

7. Coronary Artery Disease

8. Congestive Cardiac Failure

9. Valvular Heart Disease

10.Pericardial Disease / RCM / HOCM82

Physical Examination:

Height

Weight

BMI

Pulse Rate

Blood Pressure Systolic & Diastolic

JVP

CVS Heart Sounds & Murmurs Rub

RS

Lab Data:

Recent Blood Sugar Fasting/ PP / RBS

Fasting Lipid Profile

ECG

Urine Protein

ECHO

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ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர்:

வயது:

தேதி:

நோயாளி எண்:

ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கபட்டது. எனக்கு விளக்கபட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது முழு மனதுடன் சம்மதிக்கிறேன்.இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில்தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியில் இருந்து எந்தநேரமும் பின்வாங்கலாம் என்றும் அதனால் எந்தபாதிப்பும் எனக்கு ஏற்படாது என்பதையும் புரிந்துகொண்டேன். நான் என்னுடைய சுயநினைவுடன் மற்றும் முழுசுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்.

S.N	PATIENT NAME	AGE	SEX	SBP	DBP	PP	PPI	RBS	CHOLEST	LVEF	E/A	E/e'	LVDD
1	SELVAM	38	M	130	60	70	0.53846	120	180	64	1	23.6	PRESENT
2	PUGALENTHI	35	M	136	90	46	0.338235	88	138	58	0.73	14.6	ABSENT
3	SATHYA	39	F	120	70	50	0.4166666	114	150	60	0.7	13.5	ABSENT
4	YUVARAJ	29	M	120	60	60	0.5	140	170	60	1.4	19.4	PRESENT
5	KASTHURI	32	F	138	80	62	0.420289855	118	200	55	1.1	17.6	PRESENT
6	MASILAMANI	39	M	136	90	46	0.338235294	126	180	62	0.75	12.8	ABSENT
7	PERUMAL	37	M	140	70	70	0.5	126	208	56	1.7	24	PRESENT
8	RAJI	36	F	130	80	50	0.384615385	138	160	60	0.7	14.6	ABSENT
9	VELU	31	M	130	90	40	0.307692308	94	140	54	0.8	13.1	ABSENT
10	SARAVANAN	30	M	110	80	30	0.272727	108	108	62	0.8	14	ABSENT
11	MEENAKSHI	33	M	120	80	40	0.3333333	128	134	70	0.78	12.9	ABSENT
12	BASKAR	29	M	120	70	50	0.4166666	136	158	57	0.8	14.3	ABSENT
13	VINOTH	37	M	110	70	40	0.363636	78	140	54	0.75	13.8	ABSENT
14	SANGEETHA	35	F	100	60	40	0.4	156	180	65	0.8	14	ABSENT
15	MARI	39	M	126	68	58	0.46	136	168	60	1.2	16.2	PRESENT
16	SUGANYA	34	F	110	60	50	0.454545	140	187	64	0.9	15.4	PRESENT
17	PALANI	32	M	118	72	46	0.3898305	120	168	66	0.74	14.5	ABSENT
18	ARUMUGAM	38	M	120	90	30	0.25	137	150	54	0.66	13	ABSENT
19	BAAKIYAM	36	M	11O	8O	3O	0.27272	100	118	59	0.8	14.1	ABSENT
20	BABU	39	M	128	90	38	0.296875	125	146	54	0.76	13.4	ABSENT
21	RAJALAKSHMI	34	F	110	70	40	0.3636364	136	136	62	0.8	14.4	ABSENT
22	JEEVA	37	M	130	80	50	0.384165385	140	138	60	0.8	14.3	ABSENT
23	PRAVEEN	33	M	100	60	40	0.4	132	129	58	0.86	14.1	ABSENT
24	SASIKALA	38	F	110	60	50	0.454545	108	190	66	1.6	19.6	PRESENT

25	KUMAR	35	M	136	84	52	0.382352941	154	170	60	0.7	12	ABSENT
26	KALIYAMOORTHY	36	M	120	90	30	0.25	94	148	56	0.78	12.7	ABSENT
27	KAMATCHI	39	F	132	72	60	0.454545	98	186	62	1.4	20.7	PRESENT
28	GOPI	38	M	110	80	30	0.2727273	110	136	68	0.8	14.1	ABSENT
29	CHANDRASEKAR	39	M	130	90	40	0.307692308	124	164	56	0.8	14	ABSENT
30	WILSON	37	M	110	62	46	0.43636363	160	178	66	1	16	PRESENT
31	BABU	37	M	120	84	36	0.3	106	130	58	0.7	12.8	ABSENT
32	SAROJA	39	F	128	74	54	0.421875	150	190	54	1.3	18.9	PRESENT
33	MANIKANDAN	36	M	100	70	30	0.3	120	148	58	0.8	14.6	ABSENT
34	EKAMBARM	38	M	120	80	40	0.3333333	138	120	62	0.66	10	ABSENT
35	PONNI	35	F	120	68	52	0.434343	88	230	60	1.2	18	PRESENT
36	DEVAN	34	M	136	90	46	0.338235294	112	168	57	0.8	13	ABSENT
37	SINDHU	38	F	128	76	52	0.406	140	139	54	0.8	12.4	ABSENT
38	ANNADURAI	33	M	126	70	56	0.444444	154	198	54	1.5	18.3	PRESENT
39	KUPPU	37	M	116	84	32	0.275862069	120	130	62	0.7	13.8	ABSENT
40	MANIMEKALAI	36	F	120	84	36	0.3	118	128	64	0.7	12	ABSENT
41	KAVIYA	35	F	124	70	54	0.435483	120	174	60	1.3	19.4	PRESENT
42	AZHAGAR	38	M	110	70	40	0.3636364	130	140	58	0.76	14.2	ABSENT
43	RANJITH	39	M	120	90	30	0.25	96	136	59	0.8	13.3	ABSENT
44	SOORYA	35	M	132	70	62	0.46969696	138	180	56	0.9	15.6	PRESENT
45	LALITHA	38	F	134	82	52	0.388059701	114	120	64	0.8	13.2	ABSENT
46	NARAYANASAMY	39	M	110	80	30	0.2727272	120	134	54	0.8	13.3	ABSENT
47	SELLIYAMMAL	37	F	112	64	48	0.4285714	118	184	58	1.2	17	PRESENT
48	LOKESH	36	M	120	80	40	0.333333333	84	150	62	0.68	12.9	ABSENT
49	SAMPATH	39	M	130	80	50	0.384165385	132	128	58	0.9	15	ABSENT
50	KARTHIK	35	M	100	60	40	0.4	130	110	60	0.8	12.6	ABSENT