A STUDY ON THE EFFECT OF EECP ON CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF PATIENTS WITH ANGINA AND HEART FAILURE

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DEPARTMENT OF GENERAL MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 627011

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This is to certify that the dissertation entitled **"A STUDY ON THE EFFECT OF EECP ON CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF PATIENTS WITH ANGINA AND HEART FAILURE"** submitted by **Dr.V. MOHAMED IRFAN HASAN**, to The Tamil Nadu 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 my direct supervision & guidance.

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I hereby certify that this dissertation entitled **"A STUDY ON THE EFFECT OF EECP ON CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF PATIENTS WITH ANGINA AND HEART FAILURE"** is a record of work done by **Dr.V.MOHAMED IRFAN HASAN**, in the Department of General Medicine, Tirunelveli Medical College, Tirunelveli, during his postgraduate degree course period from 2016- 2019. This work has not formed the basis for previous award of any degree or diploma of this university or other.

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I solemnly declare that the Dissertation titled **A STUDY ON THE EFFECT OF EECP ON CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF PATIENTS WITH ANGINA AND HEART FAILURE** is prepared by me.

The dissertation is submitted to The Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine. I also solemnly 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 University, in India or abroad.

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PROTOCOL TITLE: AN OBSERVATIONAL STUDY ON THE EFFECT OF EECP ON CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF PATIENTS WITH HEART FAILURE AND ANGINA
PRINCIPAL INVESTIGATOR: Dr.V.MOHAMED IRFAN HASAN, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: PG STUDENT
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear, Dr.V.MOHAMED IFRAN HASAN, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.03.2017

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a) The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b) The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c) If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d) If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
   e) Approval for amendment changes must be obtained prior to implementation of changes.
   f) The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g) Any deviation/violation/waiver in the protocol must be informed.

STANDS APPROVED UNDER SEAL

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CERTIFICATE – II

This is to certify that this dissertation work titled **"A STUDY ON THE EFFECT OF EECP ON CLINICAL AND ECHOCARDIOGRAPHIC PROFILE OF PATIENTS WITH ANGINA AND HEART FAILURE"** is done by the candidate **Dr.V. MOHAMED IRFAN HASAN** with registration Number **201611356** for the award of **M.D.** Degree in the branch of **GENERAL MEDICINE (Branch I).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **6 percentage** of plagiarism in the dissertation.

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CONTENTS

ANNEXURES:

INTRODUCTION

Cardiovascular diseases are rapidly becoming the leading cause of morbidity and mortality worldwide. Even in a developing country like India, due to the emergence of Diabetes and Obesity to an epidemic proportion, the cardiovascular disease incidence is high. Patients with Ischemic Heart disease are commonly sighted like a swarm of bees, right from a rural hospital OP, to the consultation clinics of cardiac specialists in corporate hospitals.

Most patients would have a diagnosis of Chronic stable Angina with their prescription containing an armamentarium of drugs starting from Aspirin and ending with Alprazolam.These patients even though they are managed with the so called optimal medical therapy, continue to be symptomatic and have anginal episode at least once during their previous month.

Similarly, patients recovering from ischemic heart disease & patients who have suffered previous Myocardial infarction are put on standard therapy and diuretics. These patients continue to have symptoms on exertion and decreased exercise tolerance.

Further any chronic illness can lead to depression and financial burden to the family at large. Indian patients without adequate Insurance coverage were deteriorating inspite of best medical therapy.

Those ailing people and treating physicians were literally waiting for a panacea that can bring back their life to normal. A complex array of Medical & Non medical treatment options have emerged with very few being successful.

Today, among a lot of non medical treatment options, EECP stands a class apart, in managing both these patients with Stable angina & Heart Failure.EECP is the only treatment, which is completely non-invasive, effective in majority of the patients and less expensive, as it is provided as out-patient treatment and needs no hospitalization**.** It is also covered under few state run insurance schemes.

Enhanced External Counter Pulsation (EECP) therapy is the emerging new therapy, which is non-surgical; non-drug therapy which is **US FDA approved** & advised for Refractory angina and Heart Failure patients. This study evaluates the patients with Heart Failure & Angina, undergoing EECP, their clinical profile, ECHO pattern and Quality of life improvement after EECP.

The EECP device applies and releases external pressure in synchronization with the patient's cardiac cycle. When the heart is in the relaxed state, air pressure is applied sequentially from the lower legs up to the thighs to force a wave of blood pressure back to the heart, thus increasing coronary blood flow. When the heart is ejecting blood into the aorta, air is quickly released from the cuffs to remove external pressure, thus reducing the workload of the heart. The EECP therapy is for 35 days - one hour a day session for five days a week for seven weeks

AIM OF THE STUDY

- To study the Clinical Profile of patients undergoing EECP
- To study the Echocardiographic Profile of patients undergoing EECP
- To identify the outcome of EECP after a complete course of treatment
- To identify the improvement in Quality of life after EECP treatment
- To study the complications occurring during the treatment if any

REVIEW OF LITERATURE

Cardiovascular Diseases (CVD) are the Major cause for Morbidity and Mortality in world. It has become the leading cause of death worldwide. Roughly, one third of world's death is due to Cardiovascular diseases.

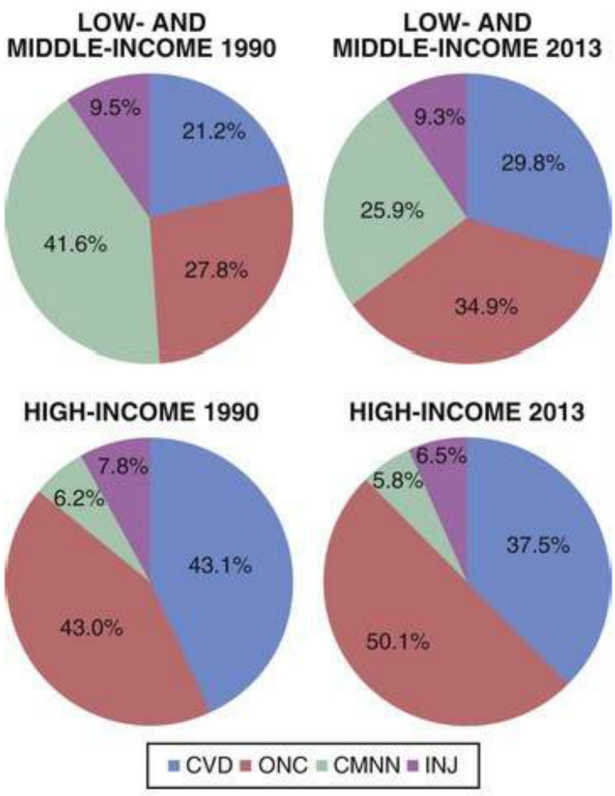
High-income countries have experienced increased rate of deaths in the past century. Now a days, even low- and middle-income countries are experiencing an alarming and accelerating increase in CVD.

Apart from Acute Coronary Syndrome, which encompasses the majority of deaths related to cardiovascular diseases, two important disease conditions add to the morbidity and significantly impair the Quality of life of the patient. They are Heart Failure and Angina. Coronary Artery Heart Disease (CHD) is an important forerunner for these two conditions.

Both these conditions lead to significant impact on economic condition and social life of the patient.

GLOBAL BURDEN OF HEART DISEASE:

CVD causes the highest number of deaths in many low- and middle-income regions, except the sub-Saharan Africa region, where it is the leading cause of death in people more than 45 years of age [1].



CVD, Cardiovascular disease;

ONC, other noncommunicable diseases;

CMNN, communicable, maternal, neonatal, and nutritional diseases;

INJ, injury

FIG.1: Changing pattern of mortality, 1990 to 2013

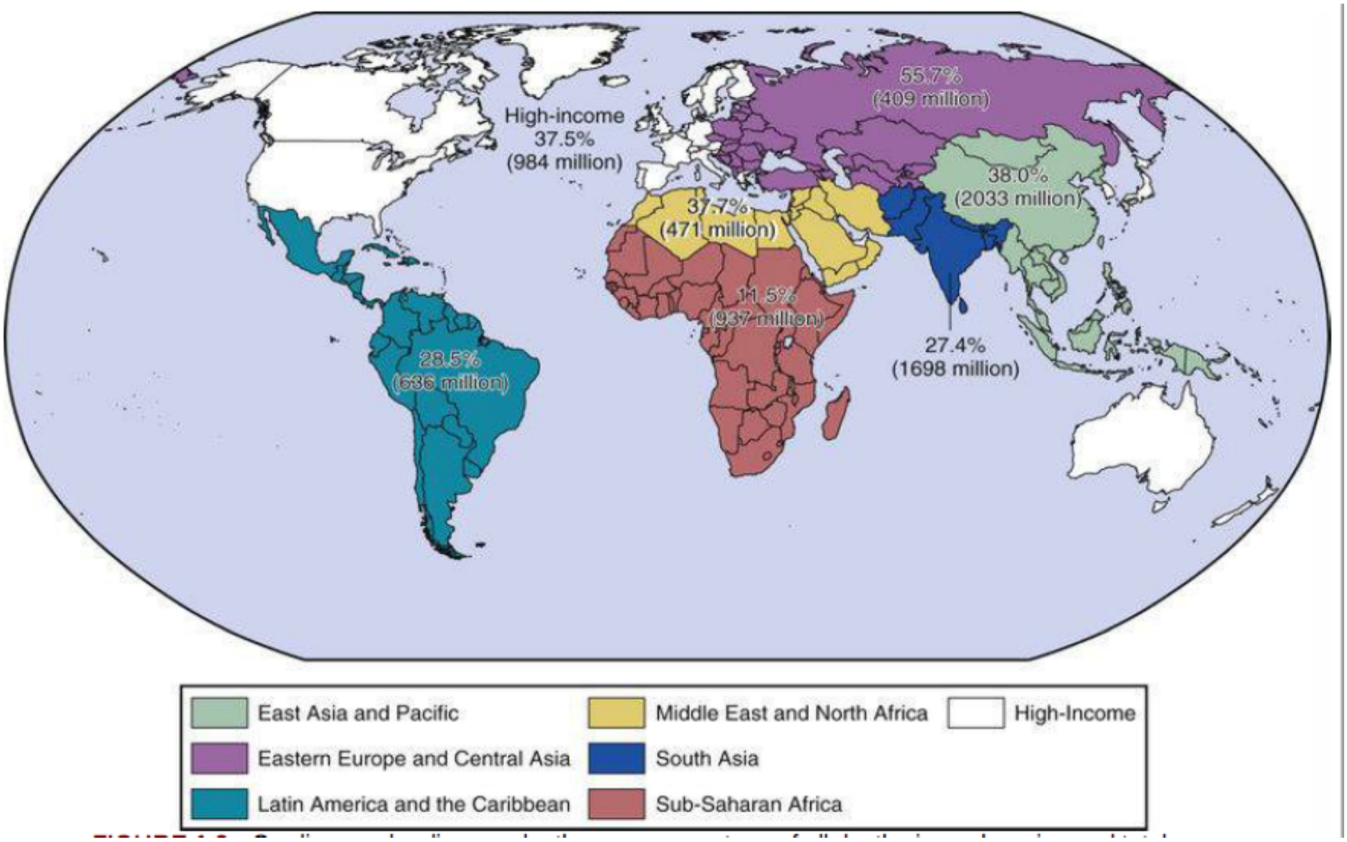


FIG.2: Cardiovascular disease deaths as a percentage of all deaths in each region and total regional population, 2013 [2].

The following factors increase the incidence of Coronary Artery Heart Disease (CHD) worldwide:

1. High fat and caloric intake and decreased physical activity lead to emergence of hypertension and atherosclerosis; also increased life expectancy. Hence mortality from chronic, noncommunicable diseases like CVD exceeds mortality from malnutrition and infectious diseases.
2. Better treatment and prevention efforts help avoid deaths among those with CVDs and caner and delay primary events.
3. Increased prevalence of obesity and diabetes

BURDEN OF DISEASE IN INDIA:

India has low life expectancy of approximately 65 years. India's GNI per capita of $1410 and is approximately averaging regional data of $1299, ranging from $540 in Nepal to $6530 in Maldives. Expenditure on Healthcare is $31, or 5% of its GDP. Neighbouring countries with lowest expenditures for health care are Pakistan and Bangladesh, with $22 and $23 per capita respectively [3].

CVD represents 31% of all deaths in India. Studies show a higher CHD prevalence in men and in urban residents. The rise in CHD mortality brings economic burden in the Indian people. Data indicate that symptoms of CHD arise 5 to 10 years earlier in this region than in Western European and Latin American countries

RISK FACTORS FOR CHD:

The aetiology of CHD is multifactorial. Apart from the obvious ones such as increasing age and male sex, studies have identified several important "risk" factors Some of the risk factors are modifiable, others are immutable/non modifiable. Presence of any of the risk factors places an individual in a high-risk category for developing CHD. The greater the number of risk factors present, the more likely one is to develop CHD. The principal risk factors called Conventional Risk factors are discussed below:

MODIFIABLE RISK FACTORS	NON MODIFIABLE RISK FACTORS
Cigarette smoking	**Age**
High blood pressure	**Sex**
Elevated serum cholesterol	**Family history**
Diabetes	**Genetic factors**
Sedentary habits	**Personality**
Stress	

Smoking:

Smoking is a uniquely human habit. Smoking has been identified as a major CHD risk factor with several possible mechanisms:

- carbon monoxide in smoke induces atherogenesis

- nicotine stimulation of adrenergic nerves raises both blood pressure and myocardial oxygen demand

- altered lipid metabolism with fall in "protective" lipids - high-density lipoproteins

It has been studied that in countries in which smoking is a prevalent habit, it is causing 25 per cent of CHD deaths in men under 65 years of age. Cigarettes are particularly important in causing sudden death from CHD more seriously in men under 50 years of age.

The Risk of developing CHD is directly related to the number of cigarettes smoked per day. Contrary to the popular belief, filter cigarettes are also not protective. Adequate data are lacking to assess long-term the patterns of e-cigarette use and the harmful effects or the beneficial effects on smoking cessation. Recently U.S. Preventive Services Task Force have concluded that the current evidence is insufficient at this time to recommend electronic nicotine delivery systems for cessation of tobacco in adults [4].

It has been proved beyond doubt that the influence of smoking is not only independent of, but also synergistic with other risk factors such as hypertension and

elevated serum cholesterol. That is the effects are more than additive, when the person with risk factor also smokes.

Smokers who quit smoking in any form surprisingly reduce their excess risk of a coronary event by 50% within the first 2 years after cessation, with majority of this benefit seen even within the first few months. CHD risk falls substantially within 1 to 2 years of cessation, with the risk of coronary event in former smokers approaching that in non-smokers after 3 to 5 years. Likewise, the risk of stroke event decreases steadily after smoking cessation, with former smokers having the same stroke risk as in non-smokers after 5 to 15 years.

Hypertension:

Elevated blood pressure is a major risk factor for CHD, heart failure, cerebrovascular disease, peripheral arterial disease, atrial fibrillation, renal failure and total mortality, as well as gradual loss of cognitive function and increased incidence of dementia.

The blood pressure is the important diagnostic utility for identifying individuals at high risk of developing CHD. Hypertension importantly accelerates the atherosclerotic process, especially if hyperlipidemia is coexistent and contributes to CHD.

In patients of age 40 to 70 years, each increment of 20 mm Hg in systolic or 10 mm Hg in diastolic BP doubles the risk of CHD across a wide BP range of 115/75 to 185/115 mm Hg [5].

Prehypertension, defined as systolic BP of 120 to 139 mm Hg or diastolic BP of 80 to 89 mm Hg, is associated with twice the risk of MI and stroke in women compared with normal BP.

In the past decade, more emphasis was placed on the importance of diastolic blood pressure. But now researchers identified that systolic blood pressure is a better predictor of CVD than is the diastolic. However, both systolic and diastolic components are significant risk factors.

Ambulatory monitoring of BP over 24 hours may provide a stronger predictor of cardiovascular morbidity and mortality than office-based measures.Comparing office with home BP measurement and self-measurement of Blood Pressure allowed identification of persons with "white coat hypertension", but did not significantly improve overall management or alter objective measures of compliance, such as left ventricular mass. In a recent Dallas Heart Study, it has been found that both white-coat hypertension (elevated office BP with normal ambulatory BP) and masked hypertension (elevated ambulatory BP with normal office BP) were associated independently with increased aortic stiffness, renal damage, and incident vascular events.

Serum Cholesterol:

The risk of CHD rises steadily with the serum cholesterol concentration. The Seven Countries Study begun in 1957 in seven countries – U.S, Greece, Italy, Netherlands, Finland, Yugoslavia, Japan - showed that elevated serum cholesterol concentration is an important risk factor for the incidence of CHD at levels of 220

mg/dl or more. This supports the notion of a "threshold level" of cholesterol, above which there is an association.

The levels of low density lipoprotein (LDL) cholesterol is directly associated with CHD. While very low-density lipoprotein (VLDL) has also been shown to be associated with premature atherosclerosis, it is significantly associated with peripheral vascular disease (intermittent claudication) than with CHD.

High-density lipoprotein (HDL) cholesterol is protective against the development of CHD - the higher its mean level in a group of individuals, the lower the incidence of infarction in those individuals. Normal HDL levels should be more than 40 mg/dl.

To further improve CHD risk prediction based on serum lipid levels, a total cholesterol/HDL ratio has been devised. A ratio of less than 3.5 has been proposed as a clinical goal for both men and women for CHD prevention.

In Humans, mutations that produce hypercholesterolemia leads to accelerated atherosclerosis as early as the first decade of life in patients with homozygous familial hypercholesterolemia, while in those with heterozygous hypercholesterolemia disease develops approximately 10 to 15 years later. These observations have led to the useful concept of a threshold cumulative lifetime exposure to LDL cholesterol that, when exceeded, results in clinically evident atherosclerosis.

Recently with new techniques, high-density and low-density lipoproteins have been subdivided into sub-fractions. The levels of plasma apolipoprotein-A-I (the major HDL protein) and apolipoprotein-B (the major LDL protein) are better

predictors of CHD than HDL cholesterol or LDL cholesterol respectively. Measurement of apolipoproteins are thus supplementing lipoprotein cholesterol determinations in assessing the risk of CHD.

Diabetes:

Insulin resistance and diabetes rank high among the major cardiovascular risk factors. These effects seem to be even larger in some ethnic minority populations and in patients with other concomitant risk factors. Surprisingly, Insulin resistance promotes atherosclerosis even before it produces frank diabetes, and it also independently increases risk for atherothrombosis. In the Emerging Risk Factors Collaboration, even small increases in fasting glucose were associated with increased rates of vascular deaths

The risk of CHD is 2-3 times high in diabetics than in non-diabetics. CHD is responsible for 30 to 50 % of deaths in diabetics above the age of 40 years in industrialized countries. Obesity and Metabolic syndrome also play a vital role in pathogenesis of inflammation [6].

Metabolic syndrome is defined a cluster of glucose intolerance and hyperinsulinemia accompanied by hypertriglyceridemia, low HDL levels, , hypertension, microalbuminuria, predominance of small dense LDL particles, and central obesity.

Genetic factors:

Family history of CHD is long known to increase the risk of premature death. A given individual's TC and LDL levels are determined by Genetic factors. However, the importance of genetic factors in the majority of CHD cases remains partly unknown.

Physical activity:

Sedentary life-style has been found associated with a greater risk of the development of early CHD. There is irrefutable data that regular physical exercise increases the concentration of HDLand decreases body weight and blood pressure, both of which are beneficial to cardiovascular health.

Hormones:

The vast difference in the mortality rates for CHD between male and female gender implies that the underlying factor may have a hormonal basis. It was hypothesized that hyperoestrogenemia may be the common underlying factor that leads both to atherosclerosis and its complications such as CHD, stroke and peripheral vascular disease

Type A personality:

Type A behaviour is associated with restlessness, competitive drive, hostility and a sense of urgency and impatience. Type-A individuals are more prone to CHD than the calmer, quieter and more philosophical Type B individuals.

Alcohol:

High alcohol intake, defined as 75 g or more per day is an independent risk factor for CHD & hypertension. The evidence that moderate alcohol intake leads to a reduction in the risk of CHD is un-substantiated.

Oral contraceptives:

Women using oral contraceptives (OCPills/OCPs) have considerably higher than normal systolic and diastolic blood pressure. The risk of myocardial infarction and thrombotic events is increased in women on oral contraceptives, and the risk is compounded by concurrent cigarette smoking.

NONCONVENTIONAL RISK MARKERS:

High-Sensitivity C-Reactive Protein

Other Biomarkers of Inflammation

Lipoprotein(a)

Homocysteine

Direct Plaque Imaging

Genetic Markers for Cardiovascular Risk

High-Sensitivity C-Reactive Protein:

Not all coronary events occur in people with conventional risk factors and in few patients, abnormalities of inflammation, hemostasis, and thrombosis appear to contribute significantly. In particular 50% of all Myocardial Infarction & Strokes occur among persons without hyperlipidemia. Thus, after conventional risk factors **atherothrombotic risk markers**, including hsCRP and other markers of inflammation, such as interleukins IL-1, IL-6, fibrinogen, and lipoprotein-associated phospholipase A2 (Lp-PLA2), as well as lipoprotein(a) (Lp[a]) assumes importance[7].

Other Biomarkers of Inflammation:

Soluble forms of certain cell adhesion molecules such as intercellular adhesion molecule (sICAM-1), P-selectin, and the mediator CD40 ligand, as well as markers of leukocyte activation such as myeloperoxidase, pregnancy-associated plasma protein A, and the IL-1 receptor family member ST2 are some of the **inflammatory biomarkers[8].** The measurement of above biomarkers can shed critical light on the atherothrombotic process.

Lipoprotein(a):

Lp(a) consists of an LDL particle with its apo B100 component linked by a disulfide bridge to apolipoprotein(a) [apo(a)], a protein sharing sequence similarity with plasminogen. Lp(a) binds and inactivates tissue factor pathway inhibitor and also augments the expression of plasminogen activator inhibitor, further linking both lipoproteins and thrombosis. Lp(a) also localizes within atherosclerotic lesions and may have critical local actions through oxidised phospholipid pathways

Homocysteine:

A sulfhydryl-containing amino acid, Homocysteine is derived from the demethylation of dietary methionine. In patients with rare inherited defects of methionine metabolism, severe hyperhomocysteinemia can develop. These patients have a greatly elevated risk of premature atherothrombosis as well as venous thromboembolism [9].

Direct Plaque Imaging:

In striking contrast with biologic factors measured in the body, **direct imaging of preclinical atherosclerosis** provides an alternative method to detect high-risk individuals who will benefit from early interventions & prevention. Even though several new imaging tests are developed, the best studied until date are ultrasound measure of the **common carotid intima-media thickness(CIMT)** and **computed tomography (CT)** to detect **coronary artery calcification(CAC)**. Both the imaging modalities can theoretically detect individuals with high CVD-risk, but both have encountered controversy in preventive cllinicalpractice[10].

With regard to CIMT, a metaanalysis of 14 population-based cohorts reported a consistent and statistically significant 9% increase in future vascular risk for each 0.1-mm increase in CIMT thickness. And CAC scanning, however, causes radiation exposure and results in increased number of further testing from unpredicted false-positive findings. Thus, whether CAC can cost-effectively improve prevention remains controversial. Although CAC scanning provides a non-invasive measure of atherosclerotic burden, patients with low calcium scores cannot be dismissed as being

at low risk. In a major study, conducted recently in currently asymptomatic individuals, 41% of all future vascular events occurred in those with a coronary artery calcium score (CACS) less than 100, and 17% occurred in those with a CACS of 0.

Genetic Markers for Cardiovascular Risk:

Inherited conditions account for up to one half of the susceptibility to coronary heart disease. Though genetic risk factors predisposing to CHD were difficult to quantify, this situation has markedly changed with the emergence of genome-wide association studies (GWASs) capable of defining highly significant risks for individual single-nucleotide polymorphisms (SNPs) common in the general population.

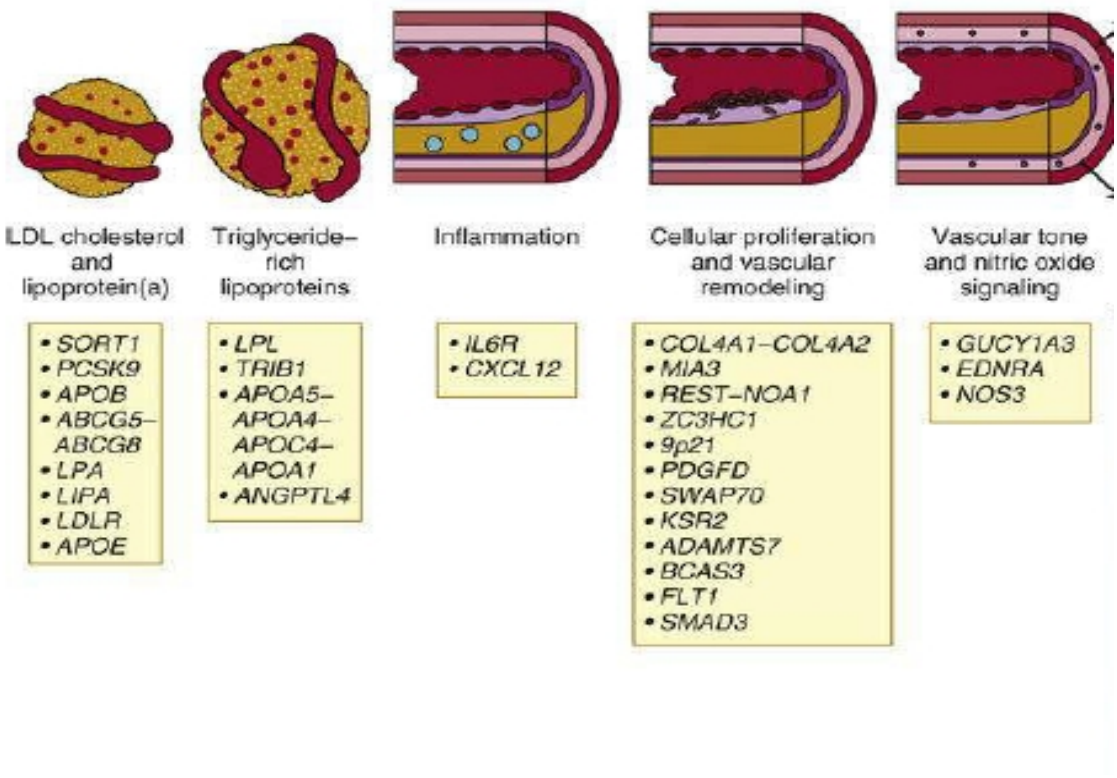


FIG.3: Genetic Factors in Cardio Vascular Disease

Alcohol Consumption:

Alcohol consumption has complex effects on CVD. Increase of daily intake from small to moderate quantities and large quantities may invert the balance between preventing and causing disease. The 2015–2020 Dietary Guidelines for Americans recommends that if alcohol should be consumed in moderation - up to one drink per day for women and two drinks per day for men—and only by adults of legal drinking age. A drink-equivalent is described using the reference beverages of 12 fl oz of regular beer (5% alcohol), 5 fl oz of wine (12% alcohol), or 1.5 fl oz of distilled spirits (40% alcohol). One drink-equivalent delivers about 12 to 14 grams of alcohol. **Habitual heavy alcohol consumption, defined as 8 or more drinks per week for women and 15 or more drinks a week for men, is one of the major cause of preventable death in many countries.** Heavy alcohol intake increases risk of total mortality, CVD mortality, stroke, fatal traffic accident, liver damage, harm in pregnancy, risk of developing breast and other cancers in both men and women, and behavioural disturbances like depression and violence.

ETIOLOGY OF CHRONIC HEART FAILURE:

- **Myocardial Disease**

Coronary artery disease

Myocardial infarction

Myocardial ischemia

Chronic pressure overload

Hypertension

Obstructive valvular disease

Chronic volume overload

Regurgitantvalvular disease

Intracardiac (left-to-right) shunting

Extracardiac shunting

Nonischemic dilated cardiomyopathy

Familial/genetic disorders

Infiltrative disorders

Toxic/drug-induced damage

Metabolic disorder

Viral or other infectious agents

- **Disorders of Rate and Rhythm**

  Chronic bradyarrhythmias

  Chronic tachyarrhythmias

- **Pulmonary Heart Disease**

  Corpulmonale

  Pulmonary vascular disorders

  High-output states

- **Metabolic Disorders**

  Thyrotoxicosis

  Nutritional disorders (beriberi)

- **Excessive Blood Flow Requirements**

  Systemic arteriovenous shunting

PATHOPHYSIOLOGY OF HEART FAILURE:

Despite repeated attempts to discover a unique pathophysiologic mechanism that can explain the clinical syndrome of heart failure (HF), no single conceptual paradigm has been established until now. Clinicians initially viewed HF as a problem of excessive salt and water retention that was caused by abnormalities of renal blood flow (cardiorenal model) & abnormal pumping capacity of the heart (cardiocirculatory model), though these models do not fully explain the disease progression that occurs in HF syndrome

Heart failure may be viewed as a progressive disorder that is initiated after an *index event* either damages the heart muscle, with a resultant loss of functioning cardiac myocytes or disrupts the ability of the myocardium to generate force, thereby preventing the heart from contracting normally. This index event may have an abrupt onset, as in the case of a myocardial infarction (MI); gradual or insidious onset, as in the case of hemodynamic pressure or volume overloading, or it may be hereditary, as in the case of many of the genetic cardiomyopathies[11].

LV remodeling alone is sufficient to cause disease progression in HF independent of the neurohormonal status of the patient.

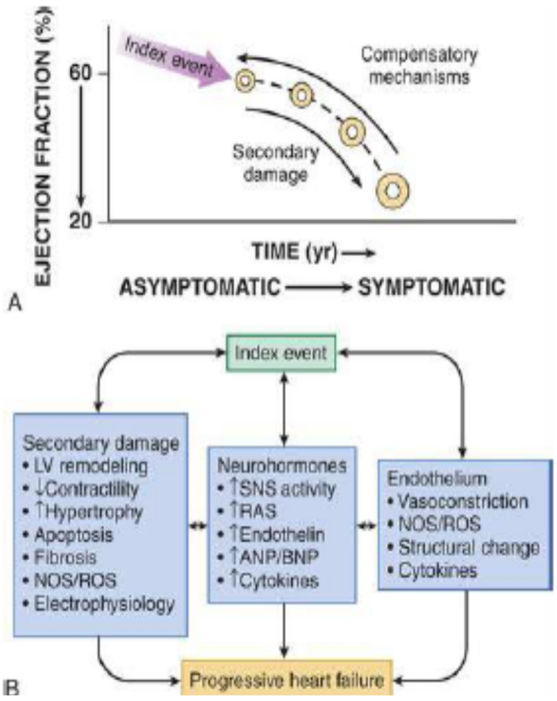
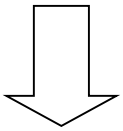
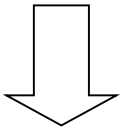


FIG.4: Pathophysiology of Heart Failure

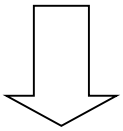
Heart failure begins after a so-called index event that produces an initial decline in pumping capacity of the heart



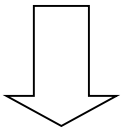
After this initial decline in pumping capacity, a variety of compensatory mechanisms are activated, including the adrenergic nervous system, the renin angiotensin system (RAS), and the cytokine systems.



In the short term, these systems are able to restore cardiovascular function to a normal homeostatic range, with the result that the patient remains asymptomatic.



With time, however, the sustained activation of these systems can lead to secondary end organ damage within the ventricle, with worsening LV remodelling and subsequent cardiac decompensation



As a result of these changes, patients undergo the transition from asymptomatic to symptomatic heart failure

Mechanical Disadvantages Created by Left Ventricular Remodelling

Increased wall stress (afterload)

Afterload mismatch

Episodic subendocardial hypoperfusion

Increased oxygen utilization

Functional mitral regurgitation

Worsening hemodynamic overloading

A stretch-induced activation of maladaptive signal transduction pathways

Stretch-induced activation of maladaptive gene programs

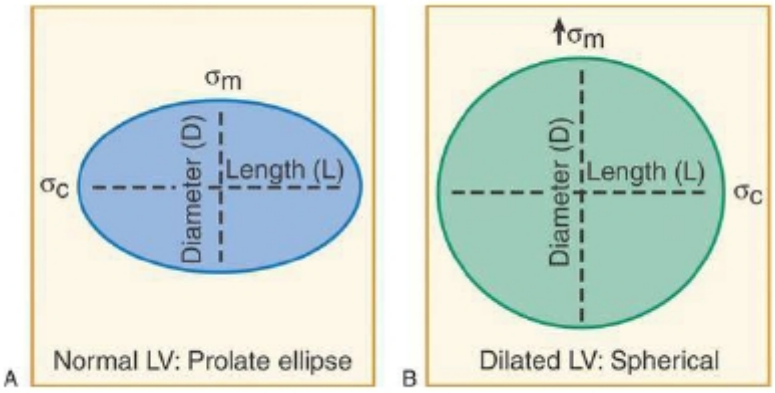


FIG.5 LV Remodelling

Reversibility of Left Ventricular Remodelling:

Clinical studies have shown that medical and device therapies that reduce HF morbidity and mortality also lead to decreased LV volume and mass and restore a more normal elliptical shape to the ventricle.Interestingly, in recognized subsets of patients, the heart undergoes reverse LV remodelling either spontaneously or after medical or device therapies. Importantly, the subsequent clinical course of these patients is associated with fewer future HF events. This phenomenon has been referred to as "myocardial recovery."

The term *reverse remodelling*, describes the biological processes involving the complete or partial reversal of the cellular, myocardial and anatomic abnormalities seen in the remodelled ventricle. Patients with hearts which have undergone reverse remodelling may experience any one of the two potential outcomes: freedom from future HF events or recurrence of HF events [12].

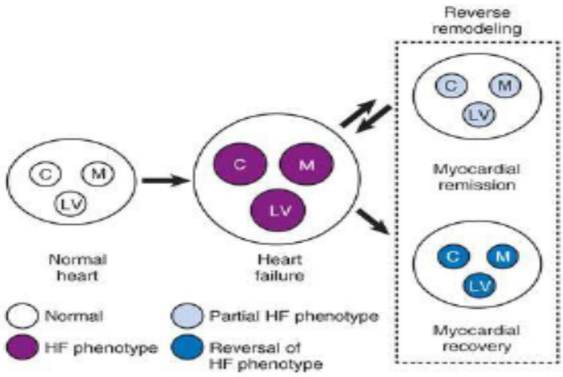


FIG.6: Reverse Remodelling

HEART FAILURE WITH PRESERVED VERSUS REDUCED EJECTION FRACTION (HFrEF vs HFpEF):

The evaluation of ejection fraction (EF) across HF patients reveals a bimodal distribution with peaks centered around 35% and 55%. About 40 to 50 % of patients have HF with preserved EF (HFpEF), and the balance have HF with reduced EF (HFrEF). HFpEF is generally defined as a left ventricular EF of 50% or greater while HFrEF is generally defined as an EF less than 40%. This stratification is important because treatment strategies for treating HF are based on these two categories. Of late interest has focused on those with HF and an EF between 40% and 50%.The concept of "midrange ejection fraction" has been proposed as an additional refinement of the standard HFrEF versus HFpEF divisions, but specific data on outcomes in HFmEF group are lacking as these patients do not yet have consensus regarding their optimal management, since they are often excluded from clinical trials

The in-hospital mortality of patients with HFpEF appears to be low when compared to that of patients with HFrEF[14]. But post discharge rehospitalisation rates are comparatively high for both groups. Patients with AHF and HFpEF are frequently rehospitalised for and die from non-cardiovascular causes than patients with HFrEF, reflecting the complexity of advanced age and greater burden of comorbidity

Common Presenting Symptoms and Signs of Decompensated Heart Failure

Fatigue

Shortness of breath at rest or during exercise

Dyspnea

Tachypnea

Cough

Diminished exercise capacity

Orthopnea

Paroxysmal nocturnal dyspnea

Nocturia

Weight gain/weight loss

Edema (of extremities, scrotum, or elsewhere)

Increasing abdominal girth or bloating

Abdominal pain (particularly if confined to right upper quadrant)

Loss of appetite or early satiety

Cheyne-Stokes respirations (often reported by family rather than patient)

Somnolence or diminished mental acuity

DIAGNOSIS OF HEART FAILURE:

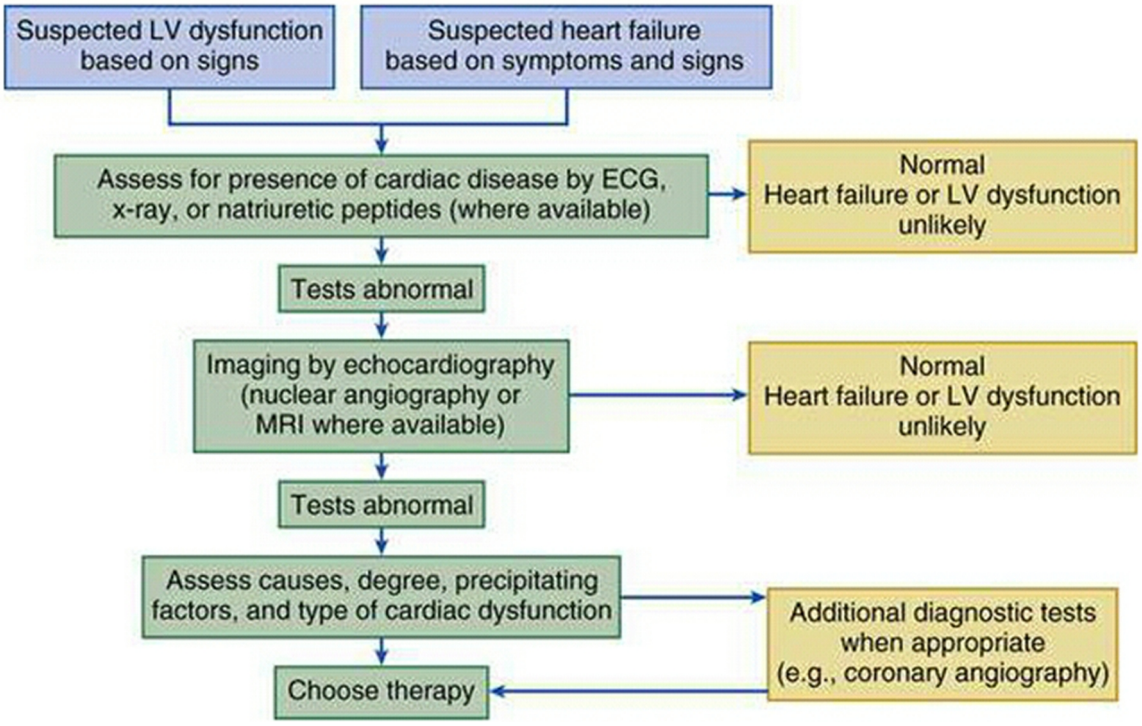


FIG.7: Algorithm for Diagnosis of Heart Failure

FRAMINGHAM CRITERIA[13]:

Diagnostic Criteria for Heart Failure (HF)
Major Criteria
Paroxysmal nocturnal dyspnea or orthopnea
Neck vein distention
Rales
Cardiomegaly
Acute pulmonary edema
S3 gallop
Increased venous pressure >16 cm H2O
Hepatojugular reflux
Minor Criteria
Ankle edema
Night cough
Dyspnea on exertion
Hepatomegaly
Pleural effusion
Vital capacity decreased One-third from maximal capacity
Tachycardia (rate >120/min)
Major or Minor Criteria
Weight loss >4.5 kg in 5 days in response to treatment

The diagnosis of HF using the Framingham criteria requires the simultaneous presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria.

FACTORS PRECIPITATING ACUTE DECOMPENSATION IN PATIENTS WITH CHRONIC HEART FAILURE (HF)

Dietary indiscretion

Inappropriate reduction in HF medications

Myocardial ischemia/infarction

Arrhythmias (tachycardia or bradycardia)

Infection

Anemia

Calcium antagonists (verapamil, diltiazem)

Beta blockers

Nonsteroidal anti-inflammatory drugs

Thiazolidinediones

Antiarrhythmic agents (all class I agents, sotalol [class III])

Anti-TNF antibodies

Alcohol consumption

Pregnancy

Worsening hypertension

STAGING OF HEART FAILURE:

ACC/AHA guidelines classify patients according to four stages, for the purpose of Guideline Directed Medical Therapy[17].

Stage A: patients at high risk for developing heart failure but without structural disorders of the heart

Stage B: patients with a structural disorder of the heart but no symptoms of heart failure

Stage C: patients with past or current symptoms of heart failure associated with underlying structural heart disease

Stage D: patients with end-stage disease who require specialized treatment strategies such as mechanical circulatory support, continuous inotropic infusions, cardiac transplantation, or hospice care

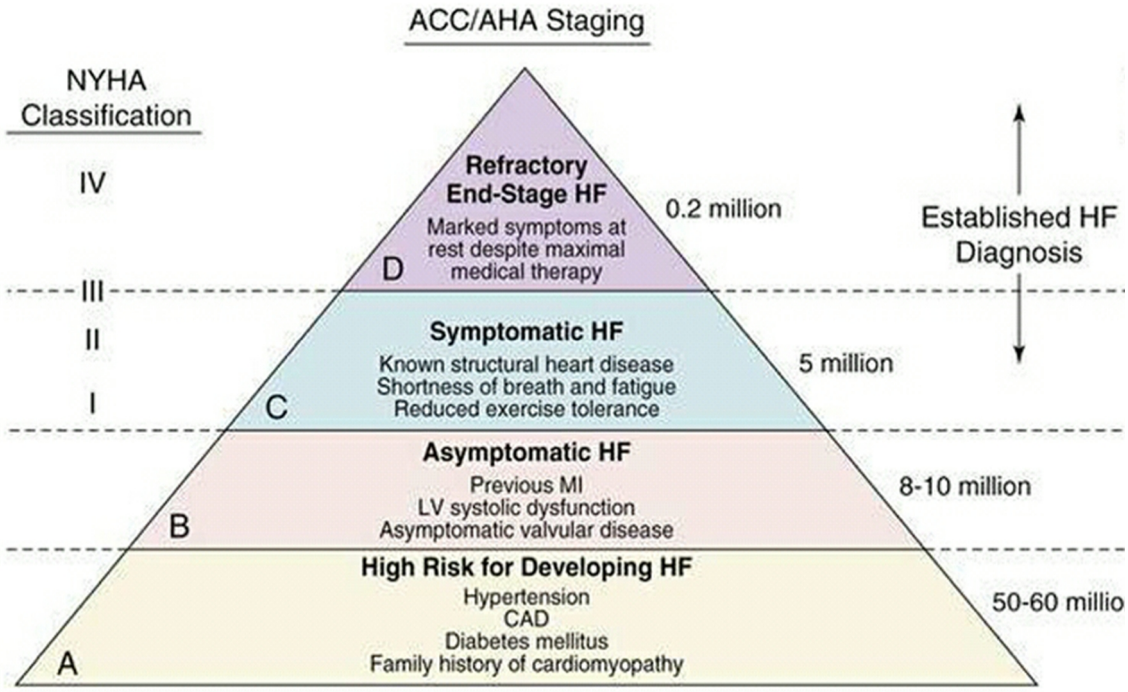


FIG.8: ACC/AHA Stages of Heart Failure and NYHA class correlation

Treatment of Patients at High Risk of Developing Heart Failure [18],[19].

(Stage A):

Strongly recommend (class I) treating **hypertension and lipid disorders** in accordance with contemporary guidelines in order to lower the risk of HF. The guidelines also suggest that other conditions that may lead to or contribute to HF, such as **obesity, diabetes mellitus**, tobacco use, and known cardiotoxic agents, should be controlled or avoided.

The updated ACC/AHA/HFSA 2017 guidelines provide a class IIa recommendation (level of evidence B-R) for the use of screening **natriuretic peptide** biomarker to prevent HF.

Treatment of Patients with Left Ventricular Dysfunction Who Have Not Developed Symptoms (Stage B):

The Aim of therapy in stage B HF is to reduce the risk of further damage to the heart and to minimize the rate of progression of LV dysfunction. If there are no contraindications, **beta blockers and angiotensin-converting enzyme inhibitors (ACEIs), or angiotensin receptor antagonists (ARBs)** in those intolerant to ACEIs, are recommended for all patients with *history of previous myocardial infarction (MI), regardless of ejection fraction (EF), and for all patients with diminished EF, regardless of history of MI.*

Guidelines discourage the use of calcium channel blockers with negative inotropic effects. The guidelines also support the use of an **ICD** in patients with

asymptomatic ischemic cardiomyopathy who have had a recent (>40 days) MI with and EF of 30% or less, who are on appropriate medical therapy, and who have a reasonable expectation of life longer than 1 year [20].

Treatment of Patients with Left Ventricular Dysfunction and

Current or Prior Symptoms (Stage C):

These stage C patients, who have current or prior symptoms attributable to LV dysfunction, require the same measures recommended for preventing or minimizing progression of LV dysfunction for stage A and B patients.

The 2017 ACC/AHA/HFSA updated guidelines support the use of **beta blockers (bisoprolol, carvedilol, sustained-release metoprolol succinate) and ACEIs** (ARBs for patients who cannot tolerate ACEIs) for all stage C patients, in the absence of contraindications, and recommend **diuretics** if needed only for patients with fluid overload. [21].

New for the 2017 guidelines is the class I recommendation (level B-R) to replace an ACE inhibitor/ARB by a **ARNI** to further reduce morbidity and mortality in patients with NYHA Class II-III heart failure. While starting an ARNI on a patient already on ACE inhibitor therapy, it is important to wait at least 36 hours, to avoid the risk of angioedema. But need not wait to start a patient already on ARB.

Also according to the 2017 AHA/ACC/HFSA guidelines, Ivabradine has class IIa recommendation for the use in symptomatic patients in sinus rhythm and a heart rate of 70/min or higher (at rest).

Based on the results of the Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS-HF), unless contraindicated MRAs are now recommended for all NYHA Class II-IV HF patients with an EF of 35% or less, to reduce morbidity and mortality [23].

Anticoagulation continues to be recommended for patients with chronic HF and permanent/persistent/paroxysmal atrial fibrillation who have an additional risk factor for cardioembolic stroke (class I, level of evidence B). Hence if additional risk factors for cardioembolic stroke are present (history of hypertension, diabetes mellitus, previous stroke or transient ischemic attack, or ≥75 years of age) patient should receive chronic anticoagulant therapy.

The **guidelines explicitly discourage the routine use of a combination of an ACEI with an ARB and MRA** because of the risk of hyperkalemia; use of an **ACEI with an ARNI** because of the risk of angioedema**; calcium channel blockers, long-term infusion of positive inotropic drugs** (except as palliation in patients with end-stage disease), **use of nutritional supplements, statins** as adjunctive therapy for HF, and **hormonal therapies** other than those needed to replete deficiencies.

Digoxin proves beneficial in patients with HFrEF, unless contraindicated, to decrease hospitalizations for HF.

Physical activity and cardiac rehabilitation are recommended for stage C patients.

Treatment of Patients with Refractory End-Stage Heart Failure

(Stage D):

Stage D has been defined by ACC/AHA as those patients with truly refractory HF who may be eligible for advanced treatment strategies such as mechanical circulatory support (MCS) procedures to facilitate fluid removal, continuous inotropic infusions, or cardiac transplantation or other novel, innovative or experimental surgical procedures, or for end-of-life care, such as hospice

DRUGS USED IN MANAGEMENT OF HEART FAILURE WITH REDUCED EJECTION FRACTION:

NEUROHORMONAL ANTAGONISM:

(ACE INHIBITION & BETA BLOCKER THERAPY)

Studies suggest a 23% reduction in mortality for heart failure in patients treated with ACEIs. viz. Lisinopril, Enalapril, Captopril, Trandolapril.

Patients treated with beta blockers (Metoprolol succinate CR/XL, Carvedilol, Bisoprolol) provide an additional 35% reduction in mortality on top of the benefit provided by ACEI therapy.

MINERALOCORTICOID ANTAGONISTS:

Aldosterone antagonism is associated with a consistent reduction in mortality in all stages of symptomatic Heart Failure with NYHA class II to IV. High levels of aldosterone in HFrEF patients promote Sodium retention, electrolyte imbalance and endothelial dysfunction and also myocardial fibrosis. The selective agent Eplerenone (studied in NYHA class II and post - MI heart failure) and the nonselective antagonist Spironolactone (studied in NYHA class III and IV HF) reduces mortality and hospitalizations, with favourable reductions in sudden cardiac death (SCD). Hyperkalemia and worsening renal function are to be watched for, especially in patients with underlying chronic kidney disease.

ARTERIOVENOUS VASODILATION

The combination of hydralazine and ISDN has been demonstrated to improve survival in HFrEF. Hydralazine reduces systemic vascular resistance and induces arterial vasodilatation by affecting intracellular calcium kinetics; nitrates are converted in smooth muscle cells into nitric oxide, which stimulates cGMP (cyclic guanosine monophosphate) production and consequent arterial-venous vasodilation. The hydralazine and ISDN combination improves survival, but not to the magnitude evidenced by ACEIs or ARBs

HEART RATE MODIFICATION

Ivabradine, an inhibitor of the If current(Funny current) in the sinoatrial node, slows the heart rate without a negative inotropic effect. The SHIFT Trial (Systolic Heart Failure Treatment with Ivabradine Compared with Placebo Trial) was

conducted in patients with class II or III HFrEF, a heart rate >70 beats/min, and history of hospitalization for heart failure during the previous year. Ivabradine reduced hospitalizations and cardiovascular death. The 2012 European Society of Cardiology (ESC) guidelines for the treatment of heart failure, suggests Ivabradine as second-line therapy before considering Digoxin in patients who remain symptomatic after guideline-based ACEIs, beta blockers, and MRAs and with residual heart rate >70/min. In patients who do not tolerate beta blockers, Ivabradine may be used with potential benefits.

DIGOXIN:

Digitalis glycosides exert a mild inotropic effect, sympathoinhibitory& attenuate carotid sinus baroreceptor activity. These effects decrease serum Norepinephrine levels, plasma renin levels & aldosterone levels. The DIG trial demonstrated a reduction in HF hospitalizations but no reduction in mortality or improvement in quality of life. Low doses of digoxin are sufficient to achieve therapeutic beneficial outcomes and higher doses breach the therapeutic safety index. Generally, digoxin is now started as a therapy for patients who remain symptomatic despite optimal therapy and adequate volume control.

ORAL DIURETICS:

Neurohormonal activation results in avid salt and water retention. Loop diuretic agents have increased potency. Clinical trial data confirming efficacy are limited, and there is no data suggest that DIuretics improve survival. Thus, diuretics should ideally be used in tailored does to avoid excessive exposure

CALCIUM CHANNEL ANTAGONISTS:

Second-generation calcium channel–blocking agents - Amlodipine and felodipine effectively reduce blood pressure in HFrEF but do not affect morbidity, mortality, or quality of life. The first generation CCB, verapamil and diltiazem, exerts negative inotropic effects and may destabilize previously asymptomatic patients. So their use is discouraged.

ANTICOAGULATION AND ANTIPLATELET THERAPY:

HFrEF is a hypercoagulable state and therefore there is a high risk of thromboembolic events, including stroke, pulmonary embolism and peripheral arterial embolism. Long-term oral anticoagulation is used in patients with atrial fibrillation; but there is insufficient evidence to support the use of warfarin in patients in normal sinus rhythm with no history of thromboembolic episodes or echocardiographic evidence of left ventricular thrombus. Aspirin blunts ACEI-mediated prostaglandin synthesis, but the clinical importance of this relation remains unclear. Current the use of aspirin is recommended in patients with ischemic cardiomyopathy.

FISH OIL:

Treatment with long-chain omega-3 polyunsaturated fatty acids (ω-3 PUFAs) has been shown to be associated with modestly improved clinical outcomes in patients with HFrEF.

IRON SUPPLEMENTS:

American Heart Association and Heart Failure Society of America (ACC/AHA/HFSA) guidelines gave a Class II b recommendation that IV iron replacement might be reasonable in patients with NYHA Class II and III HF and coexistent Iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation <20%) to improve functional status and quality of life.

ENHANCED EXTERNAL COUNTERPULSATION (EECP)[22],[23],[24] :

Non Invasive peripheral lower extremity therapy using graded external pneumatic compression at high pressure is administered in 1-hour sessions for 35 sittings over 7 weeks (5 days a week) and has been studied to reduce anginal symptoms and extend the time taken for exercise-induced ischemia in patients with CAD. The PEECH study (Prospective Evaluation of Enhanced External Counterpulsation in Congestive Heart Failure study) assessed the benefits of enhanced external counterpulsation in the treatment of patients with mild-to-moderate heart failure. This randomized trial improved exercise tolerance, quality of life, and NYHA functional classification but without an accompanying increase in peak oxygen consumption. A placebo effect due to the intervention simply cannot be excluded.

EXERCISE:

The Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) study investigated short-term (3-month) and long-term (12-month) effects of a supervised exercise training program in patients with moderate

HFrEF. They found that exercise was safe, improved the sense of well-being of the patients, their mood and correlated with a trend towards reduction of mortality.

CARDIAC RESYNCHRONISATION THERAPY (CRT):

The evidence of dyssynchrony on the surface electrocardiogram is a widened QRS interval, particularly in the presence of a left bundle branch block morphology.

Accrual of benefit in mildly symptomatic HFrEF patients occurs from applying this therapy in those with a QRS width of >149 ms and a left bundle branch bloock pattern.

SURGICAL THERAPY IN HEART FAILURE:

Coronary artery bypass grafting (CABG)

Surgical ventricular restoration (SVR),

Mitral valve Repair

Cardiac Transplantation

GENE THERAPY:

A number of trials of gene therapy have focused on post - myocardial infarction patients and have used Autologous bone marrow–derived progenitor or stem cells. These trials have had variable results. More promising results are shown by cardiac-derived stem cells, with improvement in cardiac function.

Two pilot trials delivering cells via an intracoronary approach have been studied. In one, autologous c-kit–positive cells isolated from the atria obtained from

patients undergoing CABG were cultured and reinfused. In another study,infusion of cardiosphere-derived cells grown from endomyocardial biopsy specimens were used.

SERCA2a is deficient in patients with HFrEF and is primarily responsible for reincorporating calcium into the sarcoplasmic reticulum during diastole. CUPID (Efficacy and Safety Study of Genetically Targeted Enzyme Replacement Therapy for Advanced Heart Failure) using coronary arterial infusion of adeno-associated virus type 1 carrying the gene for SERCA2a demonstrated a decrease in Natriuretic peptide levels.

CHRONIC STABLE ANGINA:

The spectrum of stable ischemic heart disease (SIHD) is broad and includes persons with chronic stable angina, asymptomatic ischemia, prior myocardial infarction, prior coronary revascularization &nonobstructive coronary atherosclerosis. SIHD is mostly caused by an atheromatous plaque that obstructs or gradually narrows the large epicardial coronary arteries. Sometimes, endothelial dysfunction, microvascular disease, and vasospasm, may exist alone or in combination with coronary atherosclerosis and can be the dominant cause of myocardial ischemia in some patients.

CHARACTERISTICS OF ANGINA:

Angina pectoris is a d**iscomfort in the chest or adjacent areas caused by myocardial ischemia**. It can be precipitated by exertion but can also be initiated by emotional distress. Angina that is prolonged, occurs at rest, or occurs in an

accelerating pattern of increasing frequency and tempo is indicative of unstable IHD, including unstable angina and acute MI

The site of the discomfort is usually retrosternal, but radiation is common and occurs along the ulnar surface of the left arm or right arm and the outer surfaces of both arms can be involved. Anginal equivalents (symptoms of myocardial ischemia other than angina), such as dyspnea, fatigue, fainting and frequent belching, are commonly seen in women and older adults. Nocturnal angina and Post prandial Angina can also occur indicating IHD[25].

A typical episode of angina pectoris begins gradually and reaches its maximum intensity over a period of minutes before dissipating. Reaching maximum severity of pain within seconds is unusual for angina pectoris. Characteristically patients with angina generally prefer to rest, sit, or stop walking during episodes[26]. Chest discomfort while walking in cold weather or walking uphill is suggestive of angina. Features suggesting the absence of angina pectoris include pain that is pleuritic, sharp or stabbing in quality, or reproduced by movement or palpation of the chest wall or arms

Typical angina pectoris is **relieved within minutes** by rest or the use of short-acting nitroglycerin. Response to Nitrates is often a useful diagnostic tool, although it should be remembered that esophageal pain may also respond to nitroglycerin. A delay of more than 5 to 10 minutes before relief is obtained with rest and nitroglycerin suggests a non ischemic cause or severe ischemia, as with acute MI or unstable angina[27].

CARDIOVASCULAR DISEASE CLASSIFICATION CHART:

Class	New York Heart Association Functional Classification	Canadian Cardiovascular Society Functional Classification
I	Patients have cardiac disease but *without* the resulting *limitations* of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.	Ordinary physical activity, such as walking and climbing stairs, *does not cause angina*. Angina present with strenuous or rapid or prolonged exertion at work or recreation
II	Patients have cardiac disease resulting in *slight limitation* of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea,oranginal pain.	*Slight limitation* of ordinary activity. Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold, or when under emotional stress or only during the few hours after wakening. Walking more than two blocks on the level and climbing more than one flight of stairs at a normal pace and in normal conditions

III	Patients have cardiac disease resulting in *marked limitation* of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.	*Marked limitation* of ordinary Physical activity. Walking one to two blocks on the level and climbing more than one flight of stairs in normal conditions
IV	Patients have cardiac disease resulting in *inability* to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.	*Inability* to carry on any physical activity without discomfort - anginal syndrome *may* be present at rest.

PATHOPHYSIOLOGY:

Angina pectoris results from myocardial ischemia, which is caused by an imbalance between myocardial O2 requirements and myocardial O2 supply. The former may be elevated by increases in heart rate (HR), left ventricular (LV) wall stress and contractility & the latter is determined by coronary blood flow and coronary arterial O2 content.

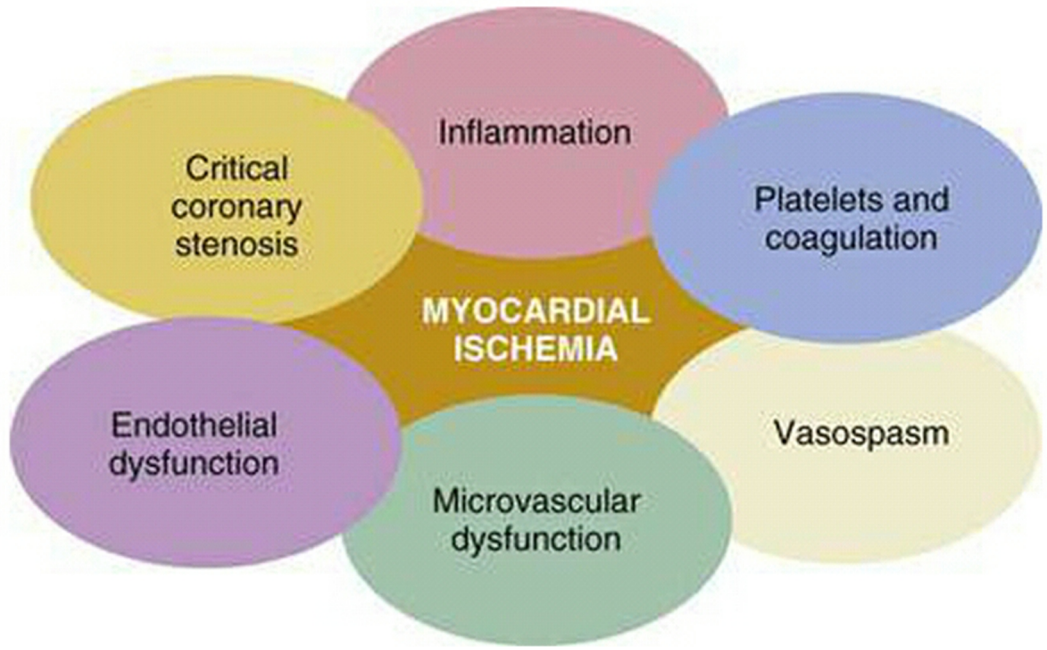


FIG.9: Pathogenesis of Myocardial Ischemia showing Non Obstructive Factors

PHYSICAL EXAMINATION:

The physical examination is usually normal in asymptomatic patients with stable angina. Due to the increased likelihood of IHD in patients with diabetes & peripheral arterial disease, clinicians should search for signs of atherosclerotic disease at other sites, such as an abdominal aortic aneurysm, carotid arterial bruits, and diminished arterial pulses in the lower extremities.

Evidence of atherosclerosis such as xanthelasmas and xanthomas, evidence for peripheral arterial disease should be sought by evaluating the pulse at multiple locations and comparing the blood pressure between the arms and between the arms and the legs (ankle-brachial index). Examination of the fundi may reveal arteriovenous nicking as evidence of hypertension. Signs of anemia, thyroid disease, and nicotine stains on the fingertips from cigarette smoking have to be searched for.

Palpation may reveal cardiac enlargement and abnormal contraction of the cardiac impulse (left ventricular dyskinesia).

Auscultation can uncover arterial bruits, a third and/or fourth heart sound, an apical systolic murmur due to mitral regurgitation and are best appreciated with the patient in the left lateral decubitus position. Aortic stenosis, aortic regurgitation, pulmonary hypertension, and hypertrophic obstructive cardiomyopathymust be excluded, since these disorders may cause angina in the absence of coronary atherosclerosis.

Examination during an anginal attack is important, since ischemia can cause transient left ventricular failure with the appearance of a third or fourth heart sound, a dyskinetic cardiac apex, mitral regurgitation, and even pulmonary edema.

Tenderness over the chest wall, localizing the discomfort with a single fingertip on the chest, or pain produced with palpation of the chest makes it unlikely that the pain is caused by myocardial ischemia.

A protuberant abdomen implies that the patient has metabolic syndrome and is at increased risk for atherosclerosis.

EVALUATION:

- **BIOCHEMICAL TESTS**

Patients with established or suspected CAD warrant evaluation of:

Total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides

Serum creatinine & estimation of glomerular filtration rate [eGFR]

Fasting blood glucose levels, and haemoglobin (Hb) A1c measurement

- **STRESS TESTING:**

- **Electrocardiographic:**

Exercise duration is usually **symptom-limited**, and the test is discontinued upon evidence of chest discomfort, severe shortness of breath, dizziness, severe fatigue, **ST-segment depression >0.2 mV** (2 mm), a fall in

systolic blood pressure >10 mmHg, or the development of a ventricular tachyarrhythmia.

The ischemic ST-segment response generally is defined as flat or downsloping depression of the ST segment >0.1 mV below baseline (i.e., the PR segment) and lasting longer than 0.08 s.

Contraindications to exercise stress testing are:

Rest angina within 48 h

Unstable rhythm

Severe aortic stenosis

Acute myocarditis

Uncontrolled heart failure

Severe pulmonary hypertension

Active infective endocarditis.

- **Cardiac Imaging:**

When the resting ECG is abnormal (e.g., preexcitation syndrome, >1 mm of resting ST-segment depression, LBBB - left bundle branch block, paced ventricular rhythm) it warrants further stress **myocardial radionuclide perfusion imaging after the intravenous administration of thallium-201 or 99m-technetium sestamibi** during exercise or pharmacologic stress.

Contemporary data also suggest **positron emission tomography (PET) imaging** (with exercise or pharmacologic stress) using N-13 ammonia or rubidium-82 nuclide as another technique for assessing perfusion.

Echocardiography is used to assess left ventricular function in patients with chronic stable angina and patients with a history of a prior myocardial infarction, pathologic Q waves, or clinical evidence of heart failure. Global and regional wall motion abnormalities of the left ventricle are assessed. Stress (exercise or dobutamine) echocardiography may cause the emergence of regions of akinesia or dyskinesia that are not previously present at rest. Stress echocardiography and stress myocardial perfusion imaging are more sensitive than exercise electrocardiography in the diagnosis of IHD.

Cardiac magnetic resonance (CMR) stress testing is also performed as an alternative to radionuclide, PET, or echocardiographic stress imaging. CMR stress testing performed with dobutamine infusion can be used to assess wall motion abnormalities accompanying ischemia, as well as myocardial perfusion.

Studies done using **Multidetector CT** detects coronary calcium and have been developed as a measure of the presence of coronary atherosclerosis. These methods involve computed tomography (CT) applications that achieve rapid acquisition of images. **Coronary calcium** detected by these imaging techniques most commonly is quantified by using the **Agatston score**, which is based on the area and density of calcification. Although the diagnostic accuracy of this imaging method is high (sensitivity, 90–94%; specificity, 95–97%; negative predictive value, 93–99%), its prognostic utility has not been defined.

➢ CORONARYARTERIOGRAPHY[28],[29] :

Coronary arteriography is used to detect or exclude serious coronary obstruction. However, coronary arteriography provides no information about the arterial wall, and severe atherosclerosis that does not encroach on the lumen may go undetected. Of note, atherosclerotic plaques characteristically are scattered throughout the coronary tree, tend to occur more frequently at branch points, and grow progressively in the intima and media of an epicardial coronary artery at first without encroaching on the lumen, causing an outward bulging of the artery—a process referred to as remodelling

Indications:

Coronary arteriography is indicated in

(1) patients with chronic stable angina pectoris who are severely symptomatic despite medical therapy and are being considered for revascularization procedure - a percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG);

(2) patients with troublesome/inconclusive symptoms that present diagnostic difficulties in whom there is a need to confirm or rule out the diagnosis of IHD;

(3) patients with known or possible angina pectoris who have survived cardiac arrest;

(4) patients with angina or evidence of ischemia on noninvasive testing with clinical or laboratory evidence of ventricular dysfunction; and

(5) patients judged to be at high risk of sustaining coronary events based on signs of severe ischemia on non-invasive testing, regardless of the presence or severity of symptoms

MANAGEMENT OF STABLE ANGINA:

Comprehensive management of Chronic Stable Angina has five aspects [31],[32]:

(1) Identification and treatment of associated diseases that can precipitate or worsen angina and ischemia

(2) Reduction of coronary risk factors

(3) Pharmacologic and non-pharmacologic interventions for secondary prevention

(4) Pharmacologic management of angina

(5) Revascularization by PCI or CABG, when indicated.

DRUGS USED FOR SECONDARY PREVENTION:

Aspirin 75 to 162 mg daily, is preferred for secondary prevention

Clopidogrel, a thienopyridine derivative, may be substituted for aspirin in patients with aspirin hypersensitivity or in those who cannot tolerate aspirin

Beta adrenoceptor–blocking drugs reduce death and recurrent MI in patients who have experienced MI & also reduce angina symptoms.

Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers. RAAS inhibitors reducing the risk for future ischemic events in some patients with CVD

Low-Dose Oral Anticoagulation

PHARMACOLOGIC MANAGEMENT OF ANGINA:

Beta Adrenoceptor–Blocking Agents

Calcium Antagonists

Nitrates

Ranolazine

Ivabradine

Nikorandil

NONPHARMACOLOGIC TREATMENT APPROACHES:

These therapies are considered only for patients who have refractory ischemic symptoms after failing optimal medical therapy with multiple agents, and coronary revascularization

Enhanced External Counterpulsation:

The use of enhanced external counterpulsation (EECP) is a non pharmacological alternative treatment of refractory Angina. EECP is generally administered as 35 sessions of 1-hour treatments over 7 weeks (5 days a week).

Several observational studies have concluded that EECP reduces frequency of angina, reduces use of nitroglycerin and improves exercise tolerance and quality of life, and these responses can last for up to 2 years [33]. In a randomized, double-blind, sham-controlled study of EECP for patients with chronic stable angina, EECP treatment was associated with an increase in time to ST-segment depression during exercise testing and a reduction in angina, as well as an improvement in health-related quality of life that extended 1 year [34]. However there are no definitive data that EECP reduces the extent of ischemia as determined by MPI.

The mechanisms underlying the effects of EECP are poorly understood. Possible mechanisms of benefits due to EECP are:

(1) Reduction in myocardial O2 demand due to durable hemodynamic changes;

(2) Improvement in myocardial perfusion caused by the capacity of increased transmyocardial pressure to open collaterals;

(3) Elaboration of various substances that improve endothelial function and vascular remodelling thereby resulting in an improvement in systemic arterial compliance.

Since most of the evidence demonstrating favourable effects of EECP is derived from uncontrolled studies [35], and data from sham-controlled studies are few, the possibility of placebo effects should be recognized.

Spinal Cord Stimulation:

Spinal Cord stimulation is an option for patients with refractory angina who are not candidates for coronary revascularization. Spinal cord stimulation is done using a specially designed electrode inserted into the epidural space. The beneficial effects of neuromodulation on pain with this technique are based on the **gate theory**, in which stimulation of axons in the spinal cord that do not transmit pain to the brain will reduce input to the brain from axons that do transmit pain. Several studies have reported variable success rates of up to 80% in terms of reducing the frequency and severity of angina. This approach should be reserved for patients in whom all other treatment options have been exhausted.

Transmyocardial Laser Revascularization:

Transmyocardial laser revascularization (TMLR) is a recent technique done by applying a laser beam on the epicardial surface of the left ventricle, approached through a lateral thoracotomy, and creating small channels from the epicardial to the endocardial surface. Early studies failed to show any benefits & hence diminished interest in TMLR. But due to its potential to enhance stem cell engraftment, new research with TMLR in conjunction with stem cell therapy are on the way.

MATERIALS AND METHODS

SOURCE OF DATA:

Patients with Chronic Angina and Heart Failure advised to undergo EECP treatment as suggested by Cardiologist, and who completes full course of treatment in our Hospital.

METHOD OF COLLECTION OF DATA:

- **STUDY TYPE:**
    - Prospective study
- **AREA OF STUDY:**
    - Cardiology & Medicine Outpatient department & wards
- **SAMPLE SIZE:**
    - 50
- **STUDY DESIGN AND SAMPLING:**
    - Cases of Chronic Stable Angina & Heart Failure selected for EECP after following Inclusion and Exclusion Criteria.

STATISTICAL ANALYSIS:

Done using simple percentage analysis, Independent t – test & one way ANOVA

- **INCLUSION CRITERIA**:

  - ✓ Known cases of Heart Failure with symptoms of Exertional dyspnoea
  - ✓ Patients with symptoms of chest pain not responding to drugs
  - ✓ Patients not opting for Coronary revascularization/surgery
  - ✓ Patients in whom coronary revascularization is unsuccessful

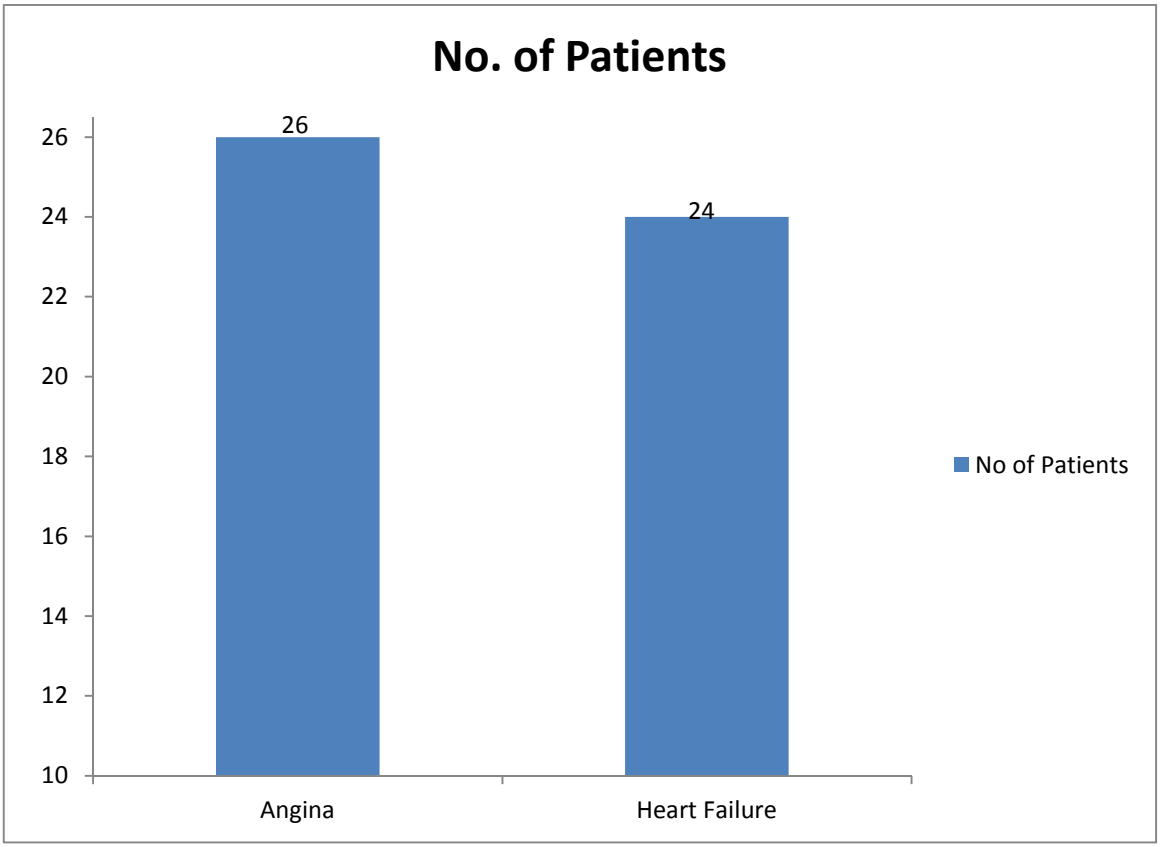
- **EXCLUSION CRITERIA:**

  - Patients with arrhythmia
  - Patients with lower limb vaso-occlusive disease
  - Patients with bleeding diathesis
  - Patients with Aortic aneurysm requiring surgical repair
  - Pregnancy
  - Uncontrolled Systemic Hypertension - SBP>180 mm Hg & DBP>120 mm Hg
  - Severe Valvular heart Disease – MS/AS/AR

OBSERVATION AND RESULTS

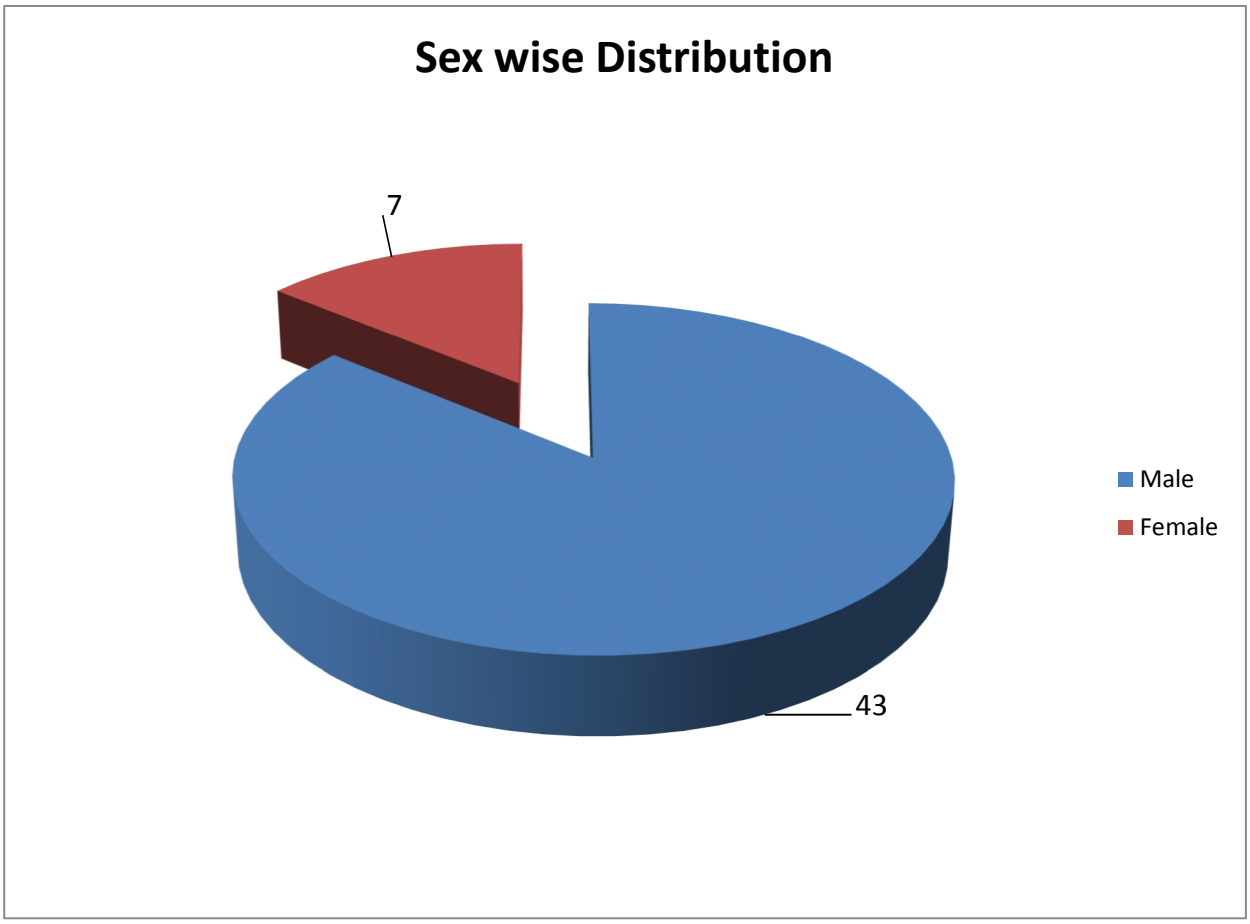
50 patients with Angina and Heart failure were enrolled for the study based on inclusion and exclusion criteria.

Table 1: STRATIFICATION OF STUDY POPULATION BASED ON DIAGNOSIS



Out of the 50 enrolled patients, 26 had Anginal Symptoms and 24 had Heart Failure symptoms.

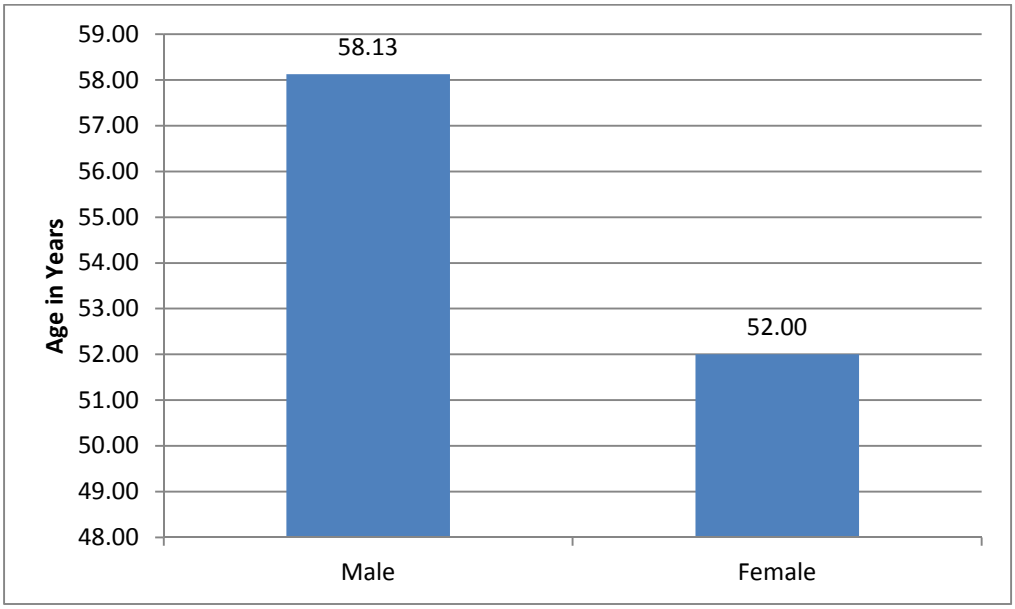
Table 2: SEX WISE DISTRIBUTION



Most of the enrolled patients were Males (86%) and 7 patients were Female (14%)

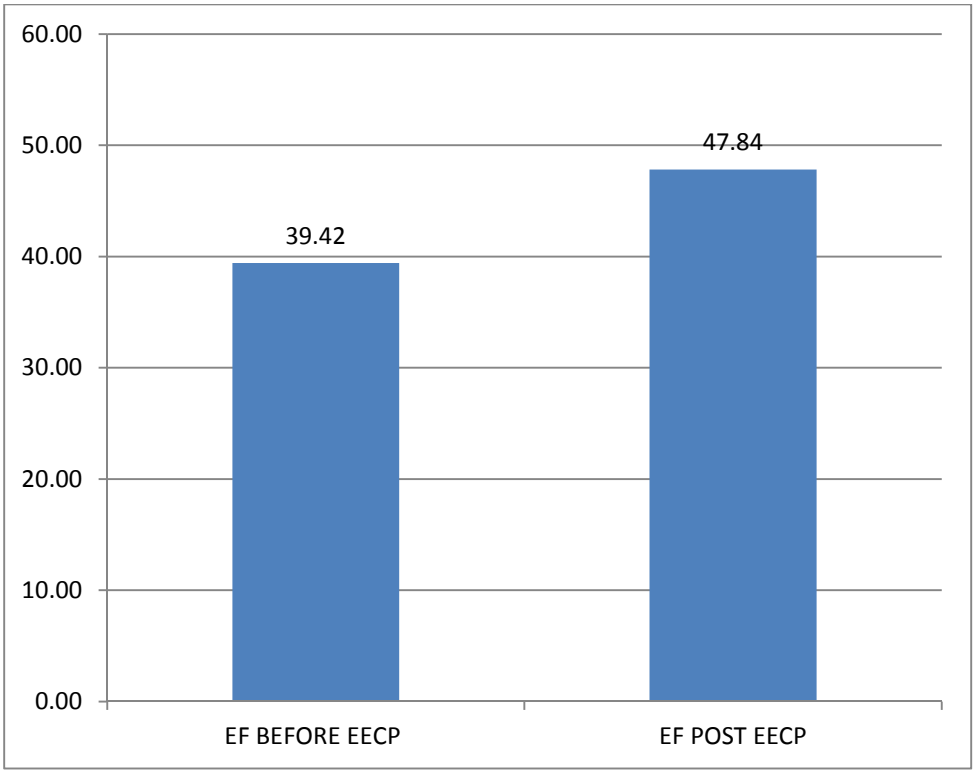
Table 3: MEAN AGE OF THE PATIENTS ENROLLED

Gender	No.	Mean Age
Male	43	58.13
Female	7	52



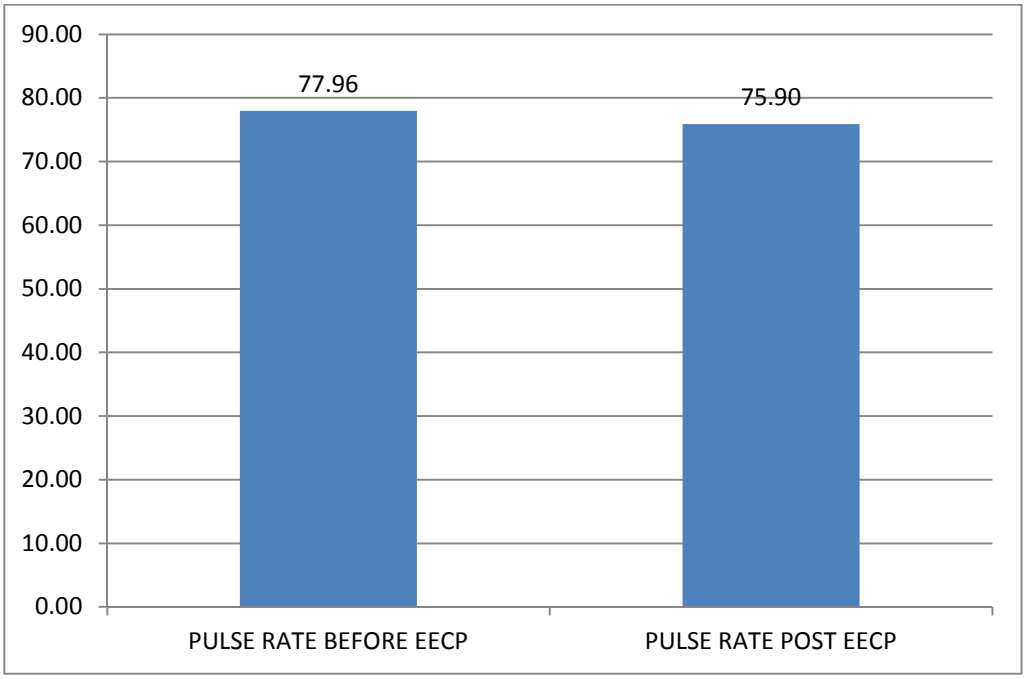
The Mean age of the male patients was 58.13 and female patients were 52 years in this study.

Table 4: EJECTION FRACTION BEFORE AND AFTER THE PROCEDURE



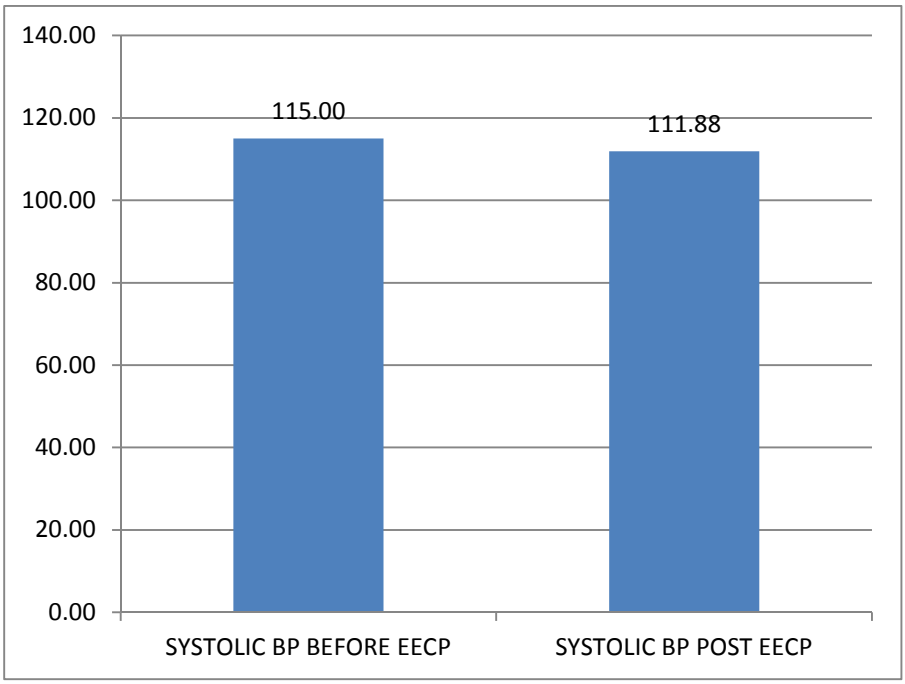
The Mean Ejection Fraction of the enrolled patients was found to be 39.42 before EECP, which improved to 47.84 measured after 35 sessions of EECP. The difference was statistically significant. ($p < 0.0001$)

Table 5: PULSE RATE VARIATION BEFORE AND AFTER THE PROCEDURE



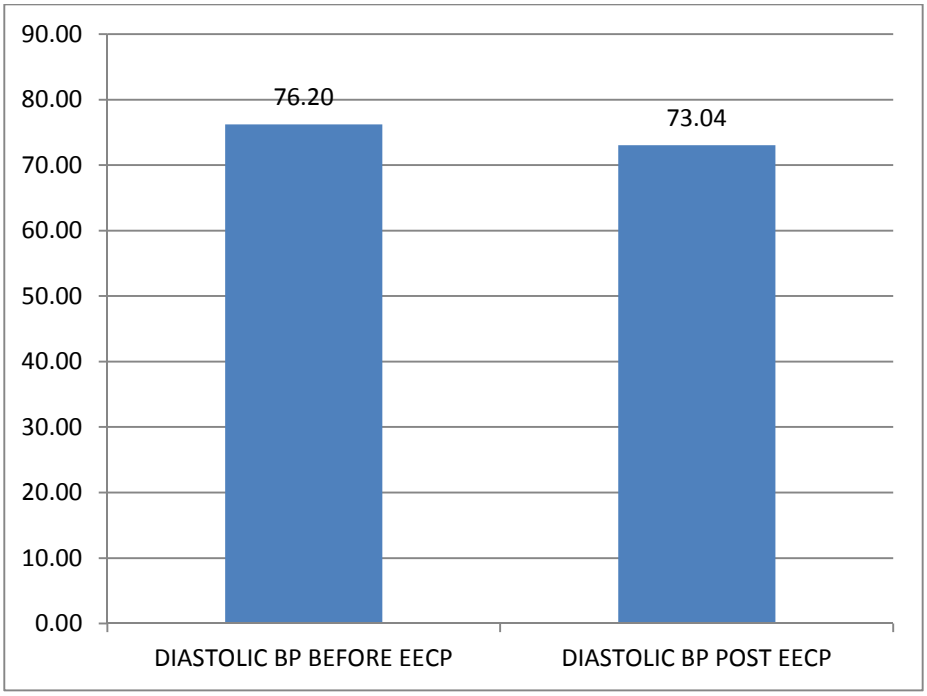
The average Pulse Rate of the enrolled patients was found to be 77.96 before EECP, which decreased to 75.90 after completing 35 sessions of EECP and the difference was statistically significant. (p value < 0.05)

Table 6: SYSTOLIC BP BEFORE AND AFTER THE PROCEDURE



The mean Systolic Blood Pressure of the patients was found to be 115 mm Hg before EECP, which decreased to 111.88 mm Hg after completion of EECP. But the reduction is statistically not significant.

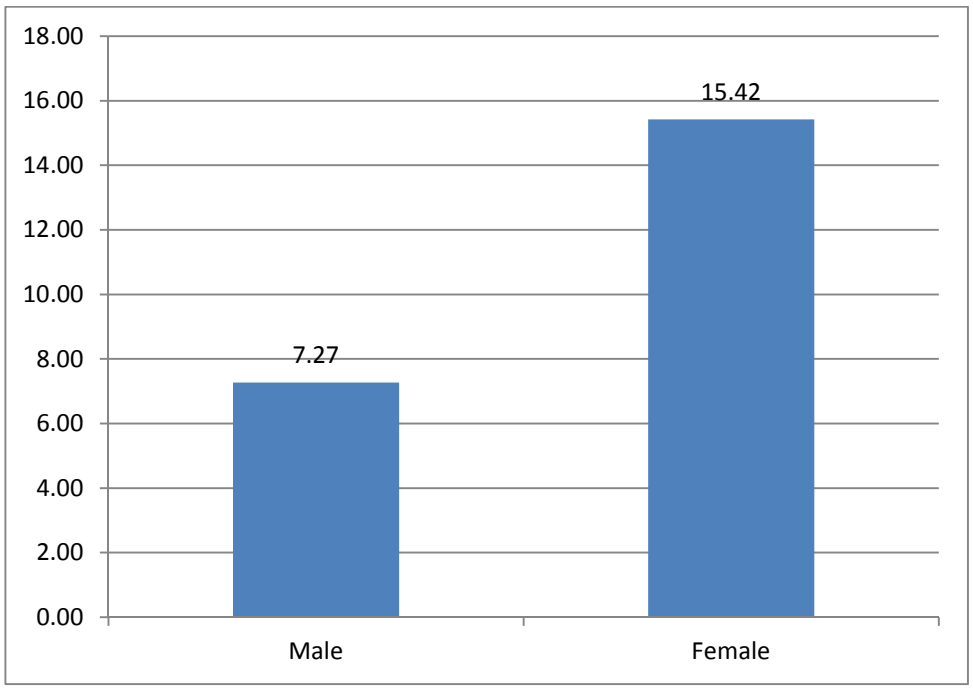
Table 7: DIASTOLIC BP BEFORE AND AFTER THE PROCEDURE



The mean Diastolic Blood Pressure of the patients was found to be 76.20 mm Hg before EECP, which decreased to 73.04 mm Hg after completion of EECP. The difference was statistically significant. (p value 0.012)

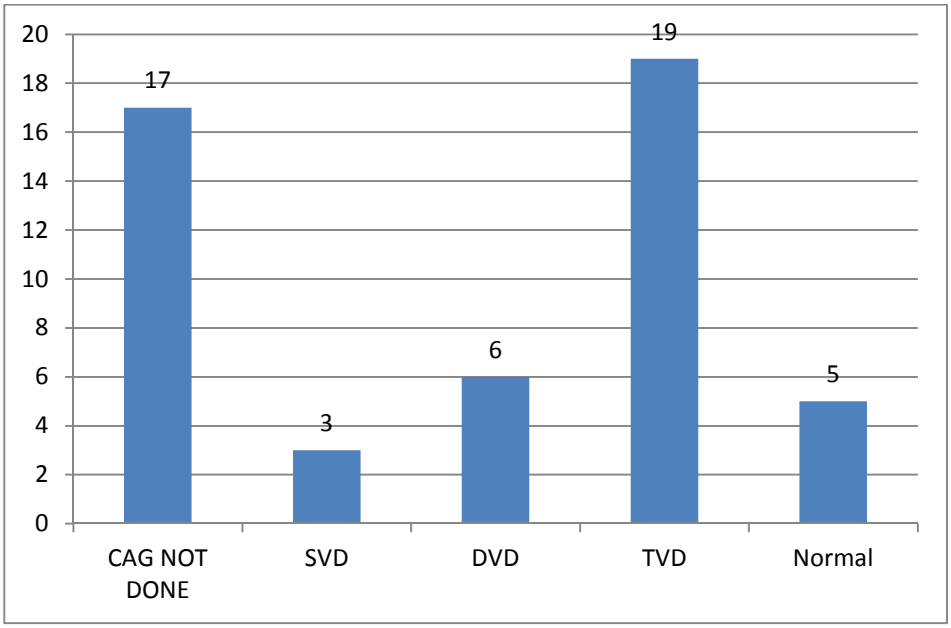
Table 8: VARIATION IN EJECTION FRACTION IN MALE & FEMALE POPULATION AFTER THE PROCEDURE

	No.	Mean	P value
Male	44	7.27	0.010
Female	6	15.42	



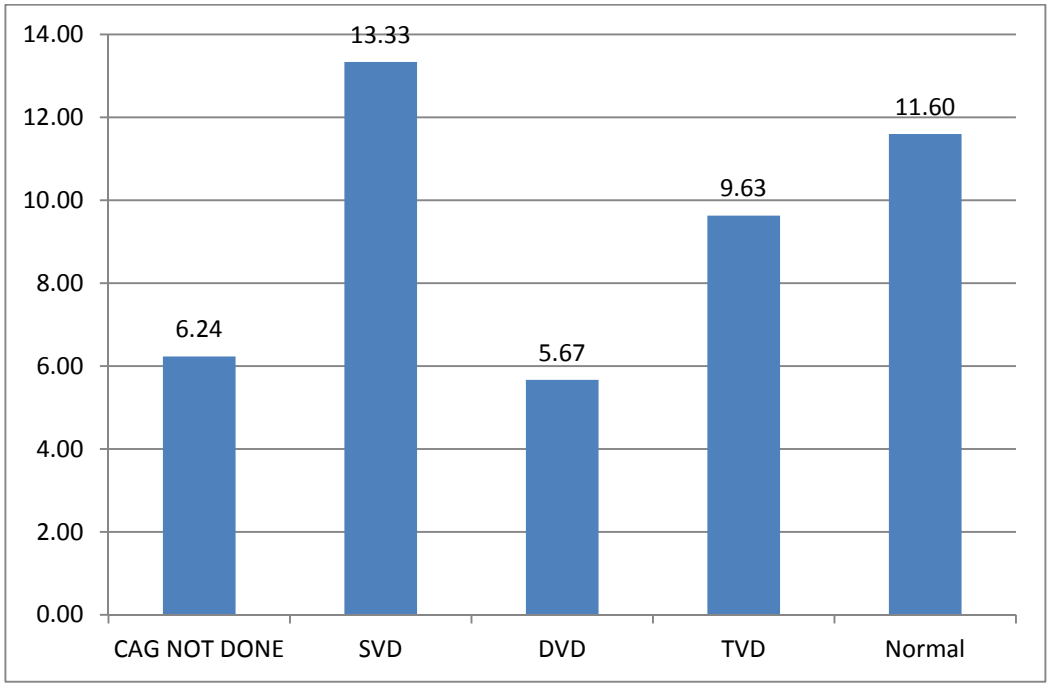
Though both male and female population had improvements in Ejection Fraction, Female patients had significantly more improvement in EF compared to male population. (P value < 0.05)

Table 9: STRATIFICATION OF STUDY POPULATION BASED ON ANGIOGRAM STUDY



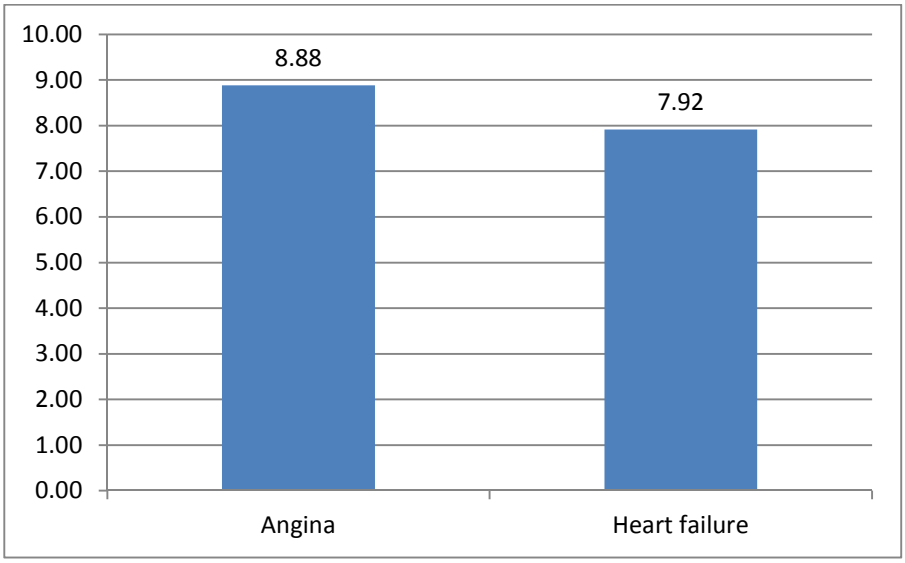
Out of the 50 study population, Angiogram was available for 33 patients. Out of which 19 had prior Triple Vessel Disease (TVD), 6 had Double Vessel Disease (DVD) and 3 had Single Vessel Disease (SVD)

Table 10: IMPROVEMENT IN EF IN VARIOUS STRATA OF CORONARY ARTERY DISEASE PATIENTS



EF improved by 13.33 in Single Vessel Disease patients, followed by 11.60 in patients with normal angiogram.

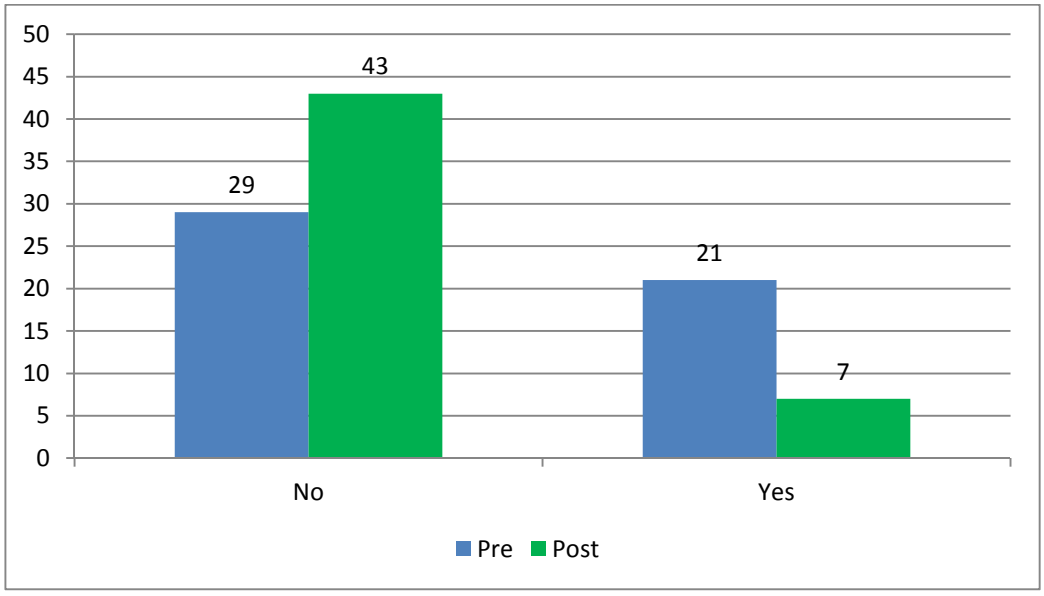
Table 11: IMPROVEMENT IN EF IN ANGINA VS HEART FAILURE SUBSETS



Patients with Angina had better improvements in EF when compared to Heart Failure subset. But the difference was not statistically significant.

Table 12: IMPROVEMENT OF ANGINAL SYMPTOMS - PRE AND POST EECP

SYMPTOMS	PRE EECP	POST EECP
No	29	43
Yes	21	7



Anginal symptoms decreased in 14 patients with symptomatic angina, 1 week after completion of EECP.

Table 13: IMPROVEMENT OF DYSPNOEA CLASS (NYHA) –

PRE AND POST EECP

		NYHA CLASS POST EECP			Total
		1.00	2.00	3.00	
NYHA CLASS PRE EECP	1.00	2	0	0	2
	2.00	20	3	0	23
	3.00	17	6	2	25
Total		39	9	2	50

Post EECP, 37 patients reverted back to Class I dyspnoea from Higher class of Dyspnoea.

Out of 25 people with class III Dyspnoea before the procedure, only 2 patients continued to be in Class III post EECP

Table 14: REDUCTION IN NITRATE DOSE - PRE AND POST EECP

		PATIENTS ON NITRATE POST EECP		
		No	Yes	Total
PATIENTS ON NITRATE BEFORE EECP	No	30	0	30
	Yes	6	14	20
Total		36	14	50

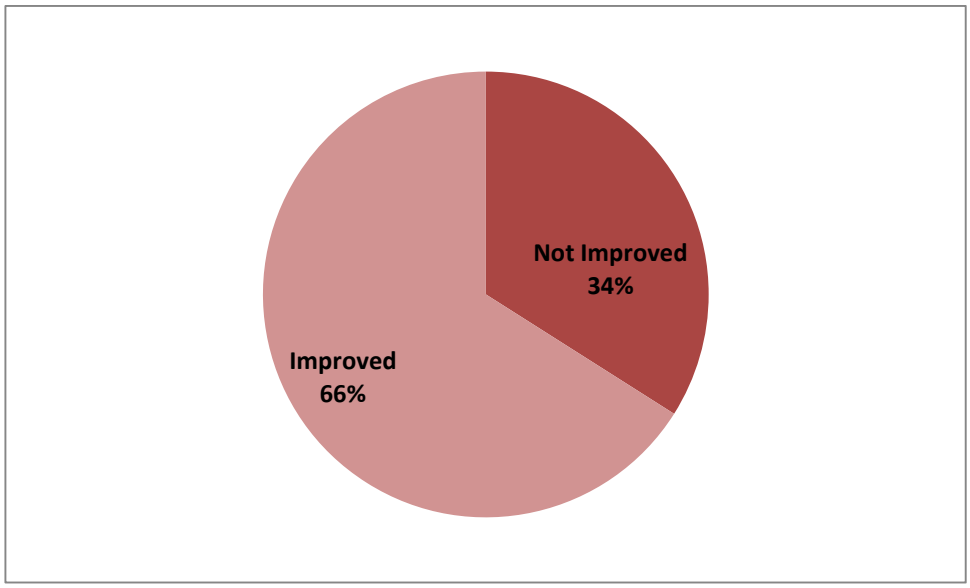
Of the 20 patients taking T.ISDN before EECP, 6 patients had withdrawn their nitrates due to regression of symptoms

Table 15: REDUCTION IN FUROSEMIDE DOSE - PRE AND POST EECP

		PATIENTS ON FUROSEMIDE AFTER EECP		
		No	Yes	Total
PATIENTS ON FUROSEMIDE BEFORE EECP	No	20	1	21
	Yes	5	24	29
Total		25	25	50

Of the 29 patients taking T. FUROSEMIDE before EECP, 5 patients had withdrawn/decreased their DIURETIC dose due to regression of congestive symptoms.

Table 16: IMPROVEMENT IN QUALITY OF LIFE POST EECP



After the completion of 35 sittings of EECP, 66% of patients enrolled had reported an Improvement in Quality of Life assessed by their ability to carry out routine day to day activities.

DISCUSSION

This observational study was conducted on 50 patients attending Medicine and Cardiology OPD and selected for EECP based on inclusion & exclusion criteria,

All patients completed the required 35 one hour sessions of EECP. They were evaluated with ECHO 1 week after the completion of EECP along with QOL questionnaire.

Out of the 50 enrolled patients, 26 had Angina inspite of optimal medical therapy and 24 had symptoms of Heart failure as assessed by Framingham criteria. Most of the study population were Male (86%) and 7 patients were Female (14%). The Mean age of the male patients was 58.13 and female patients were 52. All patients tolerated the treatment well, with no adverse events during the procedure.

The Mean Ejection Fraction of the enrolled patients was found to be 39.42 before EECP, which improved to 47.84 measured after 35 sessions of EECP. There was an improvement in EF by 8.42 after the completion of procedure. The difference was statistically significant ($p < 0.0001$).

The average Pulse Rate of the patients was 77.96 before EECP, which decreased to 75.90 after completing 35 sessions of EECP. The difference in pulse rate before and after the procedure was statistically significant with a p value of 0.028.

The mean Systolic Blood Pressure of the patients in our study was 115 mm Hg before EECP, which decreased to 111.88 mm Hg after completion of EECP. Systolic

BP decreased by more than 3 mm Hg on an average, with a p value of 0.05. The systolic BP reduction was not statistically different.

The mean Diastolic Blood Pressure of the patients in our study was 76.20 mm Hg before EECP, which decreased to 73.04 mm Hg after completion of EECP. The reduction in Diastolic BP was statistically significant with a p value of 0.012

Though both male and female population had improvements in Ejection Fraction, Female patients had significantly more improvement in EF compared to male population. (P value < 0.05)

Out of the 50 study population, Angiogram was available for 33 patients. Out of which 19 had prior Triple Vessel Disease (TVD), 6 had Double Vessel Disease (DVD) and 3 had Single Vessel Disease (SVD)

EF improved by 13.33 in Single Vessel Disease patients, followed by 11.60 in patients with normal angiogram. Even patients with TVD and patients who have undergone PCI & CABG previously, did well with this treatment.

Patients with Angina alone had better improvements in EF when compared to Heart Failure subset. But the difference was not statistically significant. Anginal symptoms decreased in 14 patients with symptomatic angina, 1 week after completion of EECP.

In patients with Dyspnoea assessed with NYHA classification, 37 patients reverted back to Class I dyspnoea from Higher class of Dyspnoea after EECP. Out of 25 people with class III Dyspnoea before the procedure, only 2 patients continued to

be in Class III post EECP. Most of the patients were in Class I Dyspnoea, 1 week after the procedure.

Then we analysed the Drug intake of the patients. After careful history and examination during the course of EECP, a stepping down of their Nitrate and Diuretic dose was done, giving importance to the volume status and Anginal symptoms. Of the 20 patients taking T.ISDN before EECP, 6 patients were withdrawn their nitrates due to regression of symptoms and continued to be symptom free, 1 week after the procedure.

Of the 29 patients taking T.FUROSEMIDE before EECP, 5 patients were withdrawn/decreased their DIURETIC dose due to regression of congestive symptoms.

After the completion of 35 sittings of EECP, 66% of patients enrolled had reported an Improvement in Quality of Life assessed by their ability to carry out routine day to day activities.

CONCLUSION

Thus according to this study, we conclude that EECP significantly reduces anginal episodes, improves failure symptoms, reduces the dose of nitrates & diuretics, and improves the quality of life of the patients. All this benefits come with a minimal risk of adverse events. An important observation in this study is that, this therapy is useful even in a case of TVD with anginal symptoms who are unsuitable for Revascularisation & also in patients who have undergone surgical revascularisation in the form of PCI or CABG and have residual disease. Several objective tests conducted by various studies also prove this with evidence. Long term follow up is needed to detect whether the benefit conferred is maintained.

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PROFORMA

Name: Age: Sex:

Occupation Residence:

Date of enrolment in EECP: OP no/ IP no.:

Indications for EECP:

Clinical history:

H/o breathlessness on exertion yes/no _____

NYHA Grade –

H/o Orthopnoea/PND yes/no _____

H/o chest pain yes/no _____

H/o palpitation yes/no _____

H/o syncope yes/no _____

H/o leg swelling yes/no _____

H/o leg pain yes/no _____

H/o abdominal distension yes/no _____

H/o limitation of day to day activities Mild/ Moderate/ Severe

Past history:

Any h/o Diabetes Mellitus/ Systemic Hypertension/ Valvular Heart Disease/ bronchial asthma/ Epilepsy/ Tuberculosis/CVA

If present, specify: _____

H/o prior EECP treatment _____

H/o Cardiac intervention PCI/CABG _____

H/o bleeding diathesis if any _____

H/o any abdominal surgery _____

H/o DVT or treatment for DVT _____

Personal history:

Diet : Smoking :

Alcohol : Drug abuse :

Drug History:

Complete list of all Cardiac drugs the patient is on -

_____ _____

_____ _____

_____ _____

_____ _____

_____ _____

Examination:

Consciousness -

Orientation -

_____ _____ _____ _____

BP : mmHg Pulse: /min RR: /min

JVP:

CVS : **RS :**

Abdomen : **CNS :**

Investigations:

ECG :

Chest X ray :

Echocardiogram :

EECP Treatment:

Duration :

Any adverse event/complication :

Compliance : Follow Up:

Patients Outcome:

POST EECP CLINICAL DATA :

H/o breathlessness on exertion yes/no _____

NYHA Grade -

H/o chest pain yes/no _____

H/o limitation of day to day physical activities Mild/ Moderate/ Severe

POST EECP ECHO CARDIOGRAM :

ANALYSIS:

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்டஅறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....

S.No	Name	Age in Yrs	Sex	CAG (SVD, DVD, TVD)	DIAGNOSIS	Anginal symptoms in the preceeding week Before EECP	Anginal symptoms 1 week after completing EECP	NYHA Dyspnoea Class Pre-EECP	NYHA Dyspnoea Class Post-EECP	EF (%) before	EF (%) after	Pulse rate before	Pulse Rate After	Systolic BP before	Diastolic BP before	Systolic BP after	Diastolic BP after	Nitrate before	Nitrate after	Furosemide before	Furosemide after	Improvement in Quality of Life
1	Selvam.T	67	M	TVD	Angina	1	1	3	1	43	46	80	72	110	70	122	68	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	1
2	Karthikeyan.S	42	M	0	Heart Failure	0	0	3	1	40	36	86	82	118	74	112	80	0	0	T.Lasix 40mg,od	0	1
3	Sargunam .S	75	M	0	Angina	1	0	2	1	27	37	105	96	98	64	128	80	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	0
4	Shahul Hameed.P	50	M	TVD	Heart Failure	0	0	2	1	51	67	76	71	130	76	110	70	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	T.Lasix 40mg,od	T.Lasix 40mg,od	1
5	Kanniapppa.R	48	M	0	Angina	1	1	3	3	32	50	83	91	116	70	100	68	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	T.Lasix 40mg,od	T.Lasix 20mg,od	1
6	Ramakrishnan.E	57	M	0	Heart Failure	0	0	3	1	60	65	90	76	136	80	116	70	0	0	T.Lasix 40mg,od	0	1
7	Syed Navas.M	32	M	0	Angina	1	1	3	2	26	26	86	83	102	68	106	68	T.Sorbitrate 5mg, tid	0	T.Lasix 40mg,bd	T.Lasix 40mg,bd	1
8	Kamaraj.A	59	M	0	Heart Failure	0	0	3	2	28	31	82	84	92	60	98	62	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	0
9	Murugaiya.s	59	M	0	Angina	1	0	3	1	33	33	80	71	130	86	120	78	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,od	1
10	Bagavathyappan.A	43	M	0	Angina	0	0	3	1	24	30	70	72	100	70	106	78	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	1
11	Oorkavalaperumal.S	33	M	Normal Coronaries	Heart Failure	0	0	2	2	41	43	61	66	104	70	108	72	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,od	1
12	Rangaraj.R	50	M	Normal Coronaries	Angina	0	0	2	1	50	76	86	88	142	100	130	90	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	T.Lasix 40mg,od	T.Lasix 40mg,od	0
13	Mani.C	56	M	Normal Coronaries	Angina	1	0	2	1	27	28	71	62	98	66	90	68	T.Sorbitrate 5mg, tid	0	T.Lasix 40mg,od	T.Lasix 20mg,od	1
14	Srinivasan.A	37	M	DVD	Heart Failure	0	0	3	1	25	30	79	85	96	64	100	64	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,bd	1
15	Bala Subramaniyan.M	33	M	Normal Coronaries	Angina	0	0	3	1	30	46	76	84	126	86	118	80	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,od	1
16	Deva Evu Manujothy	68	M	0	Heart Failure	0	0	3	2	40	53	70	72	98	68	100	66	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,bd	0
17	Backiya muthu.N	59	M	TVD	Angina	1	1	3	1	47	52	76	72	122	80	114	76	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	0
18	Paul Durai.M	59	M	0	Angina	1	0	2	1	30	37	55	64	90	64	96	64	0	0	0	0	1
19	Seyathu Ibrahim.M.A	60	M	DVD	Heart Failure	0	0	2	1	29	36	90	90	120	70	104	70	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,od	1
20	Marisamy.S	43	M	DVD	Angina	1	0	2	1	26	29	80	88	100	70	104	70	0	0	0	0	1
21	Natarajan .M	74	M	DVD	Heart Failure	0	0	2	1	68	77	74	74	132	72	130	70	0	0	0	0	0
22	Shahul Hameed.J	61	M	DVD	Angina	1	0	3	1	59	61	72	72	130	90	124	78	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	0
23	Maniammal.R	46	F	TVD	Heart Failure	0	0	2	2	43	39	80	76	90	60	106	74	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	1
24	Kother Ali .A	58	M	TVD	Heart Failure	0	0	3	1	30	39	70	68	100	70	100	68	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,od	1
25	Prema .S	60	F	Normal Coronaries	Heart Failure	0	0	2	1	27	40	72	70	140	100	122	80	0	0	T.Lasix 40mg,bd	T.Lasix 40mg,bd	1
26	Ganapathy .M	65	M	TVD	Heart Failure	0	0	3	2	50	62	88	72	100	70	112	74	0	0	0	0	0
27	Muthaiya	72	M	TVD	Heart Failure	0	0	3	2	60	66	70	66	140	100	130	82	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	T.Lasix 40mg,od	T.Lasix 40mg,od	0
28	Duwan Mydeen.P	70	M	TVD	Angina	1	0	2	1	75	72	80	76	160	100	146	70	0	0	0	0	0
29	Thanu.K	73	M	0	Angina	0	0	2	1	25	35	72	70	100	70	96	68	T.Sorbitrate 5mg, tid	0	0	0	1
30	Valli.C	52	F	TVD	Angina	1	1	2	1	27	69	70	74	120	90	112	74	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	1
31	Varataharaj.A	83	M	TVD	Heart Failure	0	0	3	1	57	64	110	95	120	80	116	80	0	0	0	0	1
32	Roja.S	42	F	SVD	Angina	1	0	2	1	60	71	96	86	110	70	120	78	0	0	0	0	1
33	Gopal.T	44	M	DVD	Angina	1	0	2	1	42	50	78	78	120	76	96	60	0	0	0	0	0
34	Mohamed kani.A.M	64	M	TVD	Angina	1	1	3	3	37	43	74	68	110	80	118	74	T.Sorbitrate 5mg, tid	0	0	0	0
35	Serma Kani.D	54	F	TVD	Heart Failure	0	0	2	1	32	47	64	68	100	70	106	70	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	1
36	Vanaja.Y	52	F	TVD	Heart Failure	0	0	3	1	38	61	72	78	130	86	110	70	0	0	0	0	0
37	Neel durai .M	65	M	SVD	Angina	0	0	2	1	30	52	74	74	100	70	114	72	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	1
38	Jeyaraj .K	65	M	0	Angina	1	0	3	1	28	33	88	82	120	80	114	74	T.Sorbitrate 5mg, tid	0	T.Lasix 40mg,od	T.Lasix 40mg,od	1
39	Velu Devar.M	67	M	0	Angina	1	0	3	2	23	28	86	80	100	70	90	60	0	0	0	0	1
40	Abu Baker.M	69	M	0	Heart Failure	0	0	2	1	34	40	102	86	100	70	100	68	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	T.Lasix 40mg,od	0	1
41	Shankaran.M	74	M	TVD	Heart Failure	0	0	2	1	32	37	64	68	110	70	110	74	0	0	T.Lasix 40mg,od	T.Lasix 40mg,bd	0
42	Dr.P Lakshmanan	70	M	TVD	Heart Failure	0	0	2	1	50	60	60	66	130	70	120	70	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	1
43	Mohan Rangan.N	55	M	0	Heart Failure	0	0	3	1	17	25	90	84	140	90	134	90	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	0
44	Venkat Rama Mahadevan.S	66	M	TVD	Angina	1	0	3	1	38	49	74	78	100	60	94	64	T.Sorbitrate 5mg, tid	0	0	T.Lasix 40mg,od	1
45	Suresh.S	48	M	TVD	Angina	1	1	2	1	62	66	82	76	120	80	114	78	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	0
46	Murugan.P	53	M	0	Heart Failure	0	0	1	1	32	41	78	72	130	90	112	78	0	0	T.Lasix 40mg,od	0	1
47	Vellaisamy.P	68	M	0	Angina	1	0	3	1	51	56	60	60	110	70	120	76	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	T.Lasix 40mg,od	T.Lasix 20mg,od	1
48	Shanmugavel.K	46	M	SVD	Heart Failure	0	0	2	2	35	42	74	75	110	80	106	76	0	0	T.Lasix 40mg,od	T.Lasix 40mg,od	0
49	Bala Subramanian.U	60	M	TVD	Heart Failure	0	0	1	1	45	53	60	60	100	60	100	60	0	0	T.Lasix 40mg,od	0	1
50	Hameethal Beevi.T	58	F	TVD	Angina	1	0	3	1	55	63	82	74	150	110	140	100	T.Sorbitrate 5mg, tid	T.Sorbitrate 5mg, tid	0	0	1

Ashok Raja	008/16	TVMCH	48	179	M	#######	#######	35	0

1	1	0	0	0	1	0	0	1	0

0	0	ICEF	0	0	0	0	0	0	3

1	0	0	0	0	0	0	0	0	0

0	0	0	28	0	0	0	0	30	99

84	112	72	105	70	67	68	0	0	0

0	0	0	0	0	0	0	0	0	oprolol 25r

T.Metoprc	0	0	T.Enalapril	T.Enalapril	T.Asprin1	T.Asprin1	0	0	T.Atorvast

T.Atorvast	T.Lasix40m	T.Lasix40m	0.8	0.9	1	1.2	1	1.5	7.6E+09

0	0	0	3	0	0	0	0	1	0