"STUDY OF CLINICAL PROFILE AND DIFFERENTIATING SYSTOLIC AND DIASTOLIC HEART FAILURE BY ECHOCARDIOGRAPHY"

By

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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

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IN

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Under the guidance of

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Signature

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ABSTRACT

"STUDY OF CLINICAL PROFILE AND DIFFERENTIATING SYSTOLIC AND DIASTOLIC HEART FAILURE BY ECHOCARDIOGRAPHY"

BACKGROUND:

Heart Failure is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. The primary manifestation of Heart Failure is dyspnoea and fatigue which leads to exercise intolerance and fluid overload which can result in pulmonary congestion and peripheral oedema. Heart Failure signs and symptoms have been classified as being due to Left ventricular failure (LVF) or Right ventricular failure (RVF). Although most patient initially have LVF, both ventricle eventually fail and contribute to Heart Failure. The aim of the current study is to evaluate the clinical profile and differentiate systolic and diastolic heart failure.

OBJECTIVES:

1) To study the clinical profile of heart failure patients.
2) To identify systolic and diastolic heart failure among those patients by Echocardiography.

MATERIALS AND METHODS:

Total 120 patients aged more than 18years and who gave informed consent, satisfying Framingham criteria for heart failure were included. Relevant history was collected and thorough clinical examination was done. Non-invasive modality like 2D echocardiography was used to assess and diastolic dysfunction. Appropriate

investigations were rendered and statistical analysis done using SPSS software version 22.0. **Chi-square test of Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data.

RESULTS:

The parameters showed majority of heart failure patients are males between age group of 51-75years.Hypertension was the most common comorbidity in these patients.50.8% of heart failure patients had reduced EF and 40.8% were with preserved EF.63.26% of the preserved EF patients were females. Presence of anemia is statistically significant ($p<0.001$). Statistical significant association was present between coronary artery disease ($P<0.001$) and reduced EF in our study. Hypertension (67.3%) was most common in patients with preserved EF. No significant association was found with symptoms and signs in both heart failure with preserved and reduced EF.

CONCLUSION

This study of clinical profiles reaffirms the value of clinical assessment in the daily practice of which increasingly includes chronic HF. Clinical profiles are easy to define, predict prognosis, and appear to do so better than traditional markers of disease severity. These profiles may be useful to guide therapy as the treatment modality differs between patients of reduced and preserved EF.

Key Words:

Heart Failure, Framingham Criteria, HFrEF, HFpEF

LIST OF ABBREVATIONS

- ACC — American College of Cardiology
- AHA — American Heart Association
- AMI — Acute myocardial infarction
- AHF — Acute Heart Failure
- BVH — Biventricular Hypertrophy
- CVD — Cardiovascular Diseases
- CMR — Cardiac magnetic resonance
- CAD — Coronary artery disease
- DPVR — Determinants of Pressure Volume Relationship
- EF — Ejection Fraction
- ESC — European society of cardiology
- HF — Heart Failure
- HFpEF — HF with preserved Ejection Fraction
- HFrEF — HF with reduced Ejection Fraction
- HFmrEF — HF with midrange Ejection Fraction
- ICD — Implantable cardioverter-defibrillator
- IHD — Ischemic Heart Disease
- LAE — Left atrial enlargement
- LAVI — Left atrial volume index
- LV — Left ventricle
- LVEF — Left ventricular ejection fraction
- LVEDV — LV end diastolic volume

- LVEDP Left ventricular end diastolic pressure
- LVM Left ventricular mass
- LVMI Left ventricular mass index
- LVESV LV end systolic volume
- LVOT LV outflow tract
- OMT Optimal Medical Therapy
- NYHA New York Heart Association
- PCWP Pulmonary capillary wedge pressure
- RAE Right Atrial Enlargement
- RVH Right Ventricular Hypertrophy
- TRV Tricuspid Regurgitation Velocity

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INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of mortality and morbidity in both developed and developing countries. Increasing life expectancy and better health care have caused heart failure (HF) to be a major public health issue, especially in older adults. India is home to 16% of global population, 25% of the world's coronary artery disease (CAD) burden, 120 million hypertensives, and a large number of individuals with Rheumatic heart disease (RHD). CVD will be the leading cause of morbidity and mortality in India by 2020.[1,2]

Heart Failure(HF) is defined, clinically, as a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function.[3] HF is not a single entity, but a clinical syndrome that may have different characteristics depending on age, sex, race or ethnicity, left ventricular ejection fraction (LVEF) status, and HF etiology. Pathophysiological differences are observed among patients diagnosed with HF and reduced LVEF compared with HF and preserved LVEF.[4]

The diagnosis of HF can be difficult. Many of the symptoms of HF are non-discriminating and, therefore, of limited diagnostic value.[5] Echocardiography plays a vital role in diagnosis of patients with heart failure, in part because the physical examination, electrocardiogram, and chest radiograph do not provide information that distinguishes diastolic from systolic heart failure.[6]

OBJECTIVES

1) To study the clinical profile of heart failure patients.
2) To identify systolic and diastolic heart failure among those patients by Echocardiography.

REVIEW OF LITERATURE

PHYSIOLOGY OF CARDIAC CYCLE [7]

The period from the beginning of one heart beat to the beginning of the next is called the **cardiac cycle**.

Each cycle is initiated by spontaneous generation of an action potential in the sinus node. The action potential travels rapidly through both atria and then through the A-V bundle into the ventricles.

Because of a special arrangement of the conducting system from the atria into ventricles, there is a delay of more than 1/10 second between passage of the cardiac impulse from the atria into the ventricles. This allows the atria to contract ahead of the ventricles, thereby, pumping blood into the ventricles prior to the very strong ventricular contraction. Thus, the atria act as primer pumps for the ventricles, and the ventricles then provide the major source of power for moving blood through the vascular system.

The cardiac cycle consists of a period of relaxation called diastole, during which the heart fills with blood followed by a period of contraction called **systole**.

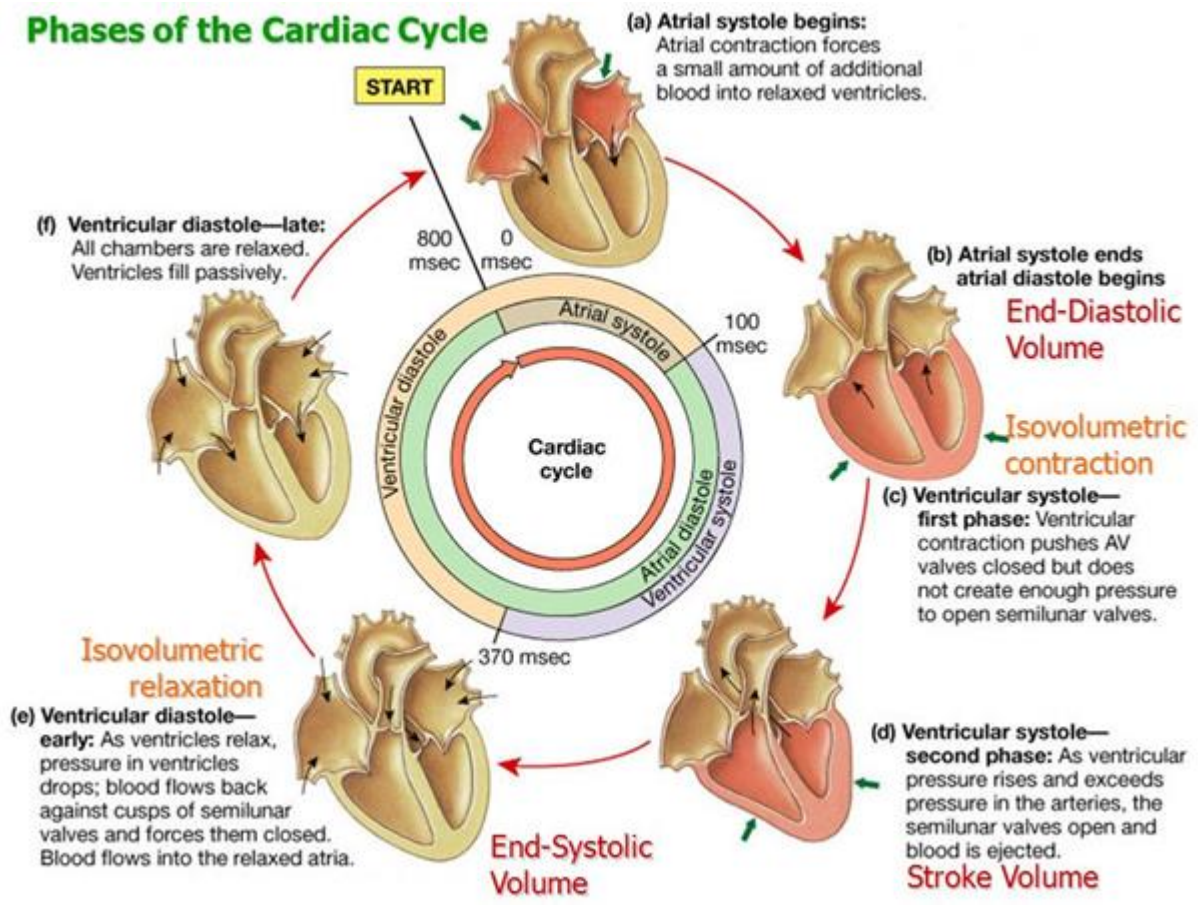


Fig 1: Phases of Cardiac Cycle

ATRIAL SYSTOLE

Blood normally flows continually from the great veins into the atria; approximately 75 percent of blood flows directly through the atria into the ventricles even before the atria contract, then atrial contraction usually causes an additional 25 percent filling of the ventricles. Therefore, the atria simply function as primer pumps that increase the ventricular pumping effectiveness as much as 25 percent.

Yet, the heart can continue to operate quite satisfactorily under normal resting conditions even without this extra 25 percent effectiveness because it normally has the capability of pumping 300 to 400 percent more blood than is required by the body anyway.

Therefore, when the atria fail to function, the difference is unlikely to be noticed unless a person exercises.

VENTRICULAR SYSTOLE

A) PERIOD OF ISOVOLUMIC (ISOMETRIC) CONTRACTION:

Immediately after ventricular contraction begins, the ventricular pressure abruptly rises causing the A-V valves to close, associated with the initial mitral component of the first heart sound. Then an additional 0.02 to 0.03 second is required for the ventricle to build up sufficient pressure to push the semilunar (aortic and pulmonary) valves open against the pressures in the aorta and pulmonary artery. Therefore, during this period of time, contraction is occurring in the ventricles, but there is no emptying. This period is called the period of isovolumic or isometric contraction, meaning by these terms that tension is increasing in the muscle, but no shortening of the muscle fibres is occurring.

B) PERIOD OF EJECTION:

When the left ventricular pressure rises slightly above 80 mm Hg (and the right ventricular pressure slightly above 80 mm Hg), the ventricular pressures pushes the semilunar valves open. Immediately, blood begins to pour out of the ventricle, with about 70 per cent of the emptying occurring during the first third of the period of ejection and the remaining 30 percent during the next two thirds.

Therefore, the first third is called the **period of rapid ejection** and the last two thirds the **period of slow ejection**. During ventricular systole, large amounts of blood accumulate in the atria because of the closed A-V valves. Therefore, just as soon as systole is over and the ventricular pressures fall again to their low diastolic values, the high pressures in the atria

immediately push the A-V valves open and allow the blood to flow rapidly into the ventricles.

C) PERIOD OF ISOVOLUMIC (ISOMETRIC) RELAXATION:

The very brief initial phase of diastole is referred to as **protodiastole** and represents the time required for the reversal of flow in the aorta and for closure of the aortic valve. The beginning of the next phase of isovolumic relaxation of the left ventricle is signified by the closure of the aortic valve, as indicated by the **second heart sound.** The elevated pressures in the distended large arteries immediately push blood back towards the ventricles, which snaps the aortic and pulmonary valves closed.

For another 0.03 to 0.06 second, the ventricular muscle continues to relax, even though the ventricular volume does not change, giving rise to the period of isovolumic or isometric relaxation. During this period, the intraventricular pressure fall rapidly back to their low diastolic levels. Then the A-V valves open to begin a new cycle of ventricular pumping.

END-DIASTOLIC VOLUME, END-SYSTOLIC AND STROKE VOLUME OUTPUT:

During diastole, filling of the ventricles normally increases the volume of each ventricle to about 100 to 120 milliliters (ml). This volume is known as the end-diastolic volume. Then as the ventricles empty during systole, the volume decreases by about 70 ml, which is called the **stroke volume output.**

Volume of blood left in each ventricle after ventricular systole, about 40 to 50 ml, is called the **end-systolic volume**.

The fraction of the end- diastolic volume that is ejected is called the **ejection fraction-** usually equal to about 60 percent.

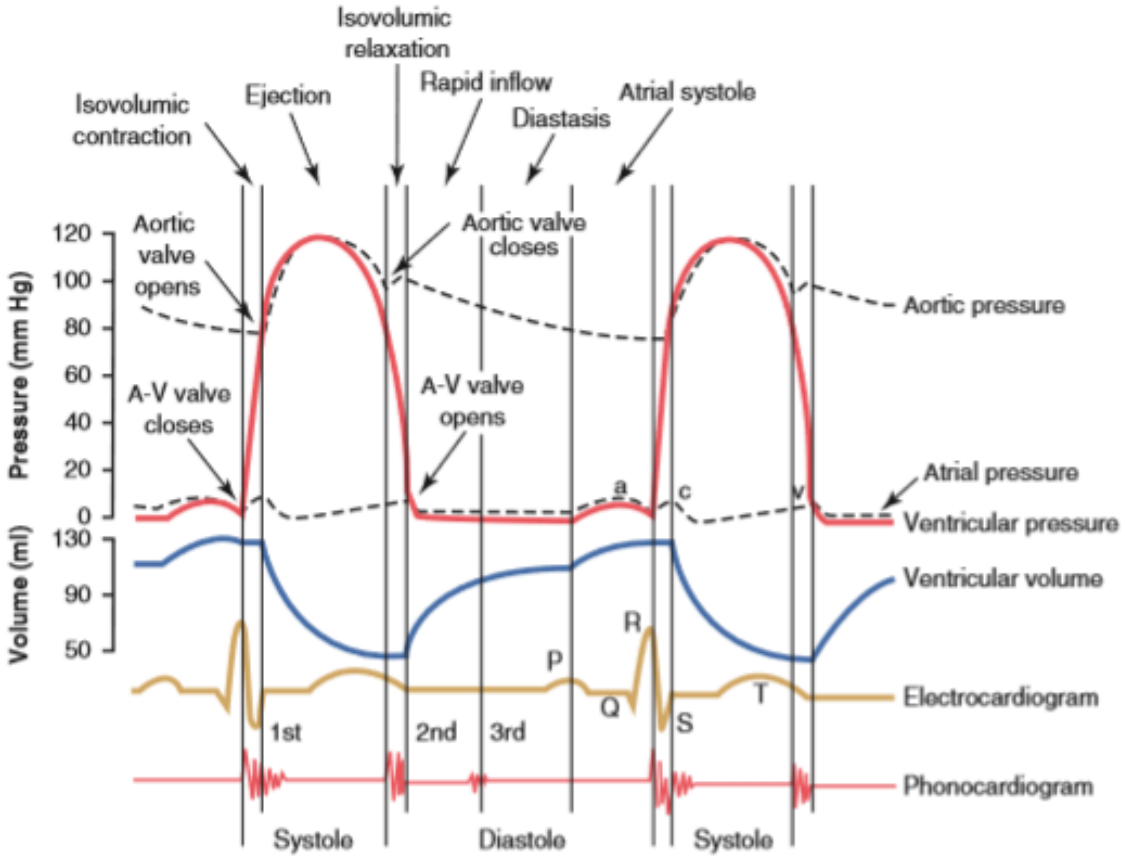


Figure 2: Events of the cardiac cycle for left ventricular function, showing changes in left atrial pressure, left ventricular pressure, aortic pressure, ventricular volume, the electrocardiogram and the phonogram. A-V denotes atrioventricular

HEART FAILURE

Heart failure(HF) is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress.[8,9]

CLASSIFICATION OF HEART FAILURE

A) TERMINOLOGY BASED ON LVEF

The main terminology used to describe HF is based on measurement of the LVEF. HF comprises a wide range of patients, from those with normal LVEF [typically considered as ≥50%; HF with preserved EF (HFpEF)] to those with reduced LVEF [typically considered as, 40%; HF with reduced EF (HFrEF)].

Table 1: Terminology Of Heart Failure Based On LVEF

HFrEF	HFmrEF	HFpEF
Symptoms+/-Signs	Symptoms+/-Signs	Symptoms+/-Signs
LVEF <40%	LVEF 40-49%	LVEF ≥50%
---	1.Elevated levels of natriuretic peptides 2.Atleast one additional criteria a)relevant structural heart disease (LVH/LAE) b) Diastolic dysfunction	1.Elevated levels of natriuretic peptides 2.Atleast one additional criteria a)relevant structural heart disease(LVH/LAE) b)Diastolic dysfunction
HFrEF-HF with reduced ejection fraction; HFmrEF-HF with mid-range ejection fraction; HFpEF-HF with preserved ejection fraction; LVH-left ventricular hypertrophy; LAE-left atrial enlargement		

Differentiation of patients with HF based on LVEF is important due to different underlying aetiologies, demographics, co-morbidities and response to therapies.[10] Most clinical trials published after 1990 selected patients based on LVEF [usually measured using echocardiography, a radionuclide technique or cardiac magnetic resonance (CMR)], and it is only in patients with HFrEF that therapies have been shown to reduce both morbidity and mortality.[11]

The diagnosis of HFpEF is more challenging than the diagnosis of HFrEF. Patients with HFpEF generally do not have a dilated left ventricle (LV), but instead often have an increase in LV wall thickness and/or increased left atrial (LA) size as a sign of increased filling pressures. Most have additional 'evidence' of impaired LV filling or suction capacity, also classified as diastolic dysfunction, which is generally accepted as the likely cause of HF in these patients (hence the term 'diastolic HF').[11]

However, most patients with HFrEF (previously referred to as 'systolic HF') also have diastolic dysfunction, and subtle abnormalities of systolic function have been shown in patients with HFpEF. Hence the preference for stating preserved or reduced LVEF over preserved or reduced 'systolic function'.[12]

According to 2012 ESC (European society of cardiology) guidelines it was acknowledged that a grey area exists between HFrEF and HFpEF.[12] These patients have an LVEF that ranges from 40 to 49%, hence the term HFmrEF. Identifying HFmrEF as a separate group will stimulate research into the underlying characteristics, pathophysiology and treatment of this group of patients. Patients with HFmrEF most probably have primarily mild systolic dysfunction, but with features of diastolic dysfunction.

B) TERMINOLOGY RELATED TO TIME COURSE OF HEART FAILURE[11]

- Patient who has never exhibited the typical symptoms and/or signs of HF and with a reduced LVEF is described as having **asymptomatic LV systolic dysfunction**.
- Patients who have had HF for some time are often said to have '**chronic HF**'.
- A treated patient with symptoms and signs that have remained generally unchanged for at least 1 month is said to be '**stable HF**'.
- If chronic stable HF deteriorates, the patient may be described as '**decompensated HF**' and this may happen suddenly or slowly, often leading to hospital admission, an event of considerable prognostic importance.
- **New-onset ('de novo')** HF may also present acutely, for example, as a consequence of acute myocardial infarction (AMI), or in a subacute (gradual)fashion, for example, in patients with a dilated cardiomyopathy (DCM), who often have symptoms for weeks or months before the diagnosis becomes clear. Patient may have HF due to problem that resolves completely (e.g. acute viral myocarditis, takotsubocardiomyopathy or tachycardiomyopathy).
- **'Congestive HF'** is a term that is used to describe acute or chronic HF with evidence of volume overload.

Many or all of these terms may be accurately applied to the same patient at different times, depending upon their stage of illness.[11]

ACC / AHA has staged Heart Failure into four stages [13]

Stage A: At risk of Heart Failure

Stage B: Asymptomatic Heart Failure

Stage C: Symptomatic Heart Failure

Stage D as Refractory Heart Failure.

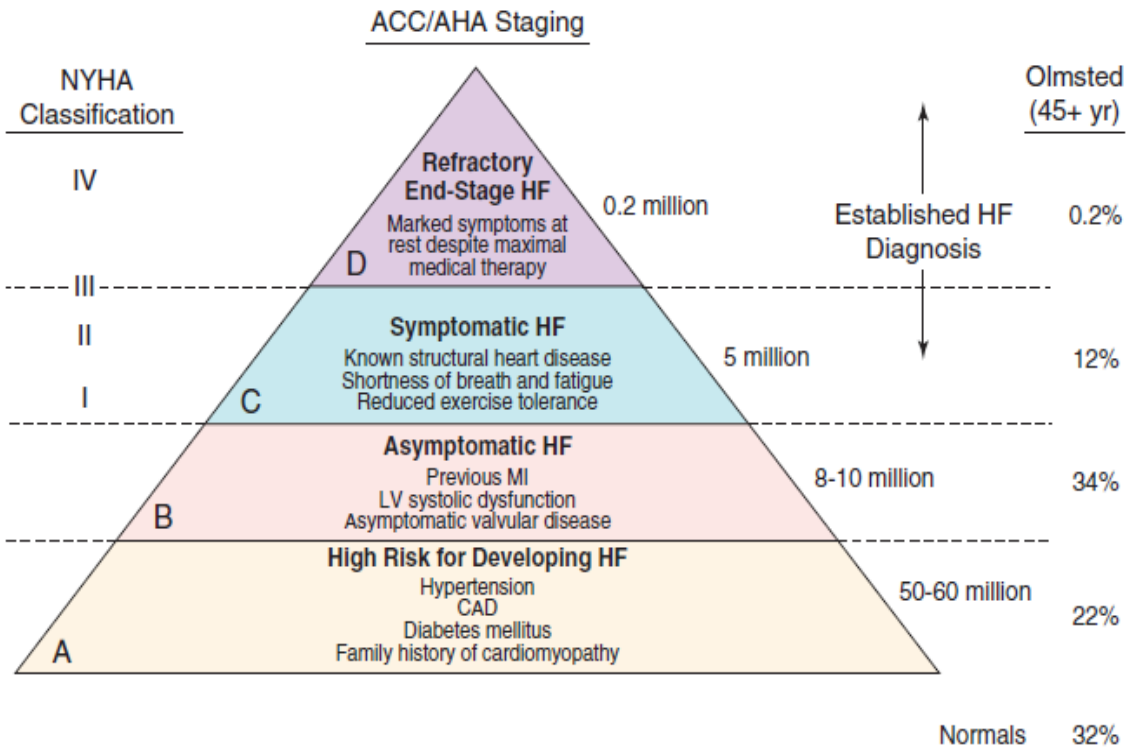


Figure 3: Stages of HF and their prevalence (data from the Olmstead County Epidemiology Study).

NYHA FUNCTIONAL CLASSIFICATION [14]

I-No limitation of physical activity, Ordinary physical activity does not cause symptoms of HF

II-Slight limitation of physical activity, Comfortable at rest, but ordinary physical activity results in symptoms of HF

III-Marked limitation of physical activity, Comfortable at rest, but less than ordinary activity causes symptoms of HF

IV-Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

C) TERMINOLOGY RELATED TO SYMPTOMATIC SEVERITY OF HEART FAILURE

The NYHA functional classification has been used to describe the severity of symptoms and exercise intolerance. However, symptom severity correlates poorly with many measures of LV function; although there is a clear relationship between the severity of symptoms and survival, patients with mild symptoms may still have an increased risk of hospitalization and death.[15]

Sometimes the term 'advanced HF' is used to characterize patients with severe symptoms, recurrent decompensation and severe cardiacdysfunction.[15]

ACUTE HEART FAILURE (AHF)

DEFINITION AND CLASSIFICATION

AHF refers to rapid onset or worsening of symptoms and/or signs of HF. AHF may present as a first occurrence (de novo) or, more frequently, as a consequence of acute decompensation of chronic HF, and may be caused by primary cardiac dysfunction or precipitated by extrinsic factors, often in patients with chronic HF.

Acute myocardial dysfunction (ischaemic, inflammatory or toxic), acute valve insufficiency or pericardial tamponade are among the most frequent acute primary cardiac causes of AHF. Decompensation of chronic HF can occur without known precipitant factors, but more often with one or more factors, such as infection, uncontrolled hypertension, rhythm disturbances or non-adherence with drugs/diet.[16]

In most cases, patients with AHF present with either preserved (90–140 mmHg) or elevated (.140 mmHg; hypertensive AHF) systolic blood pressure (SBP). Only 5–8% of all

patients present with low SBP (i.e. 90 mmHg; hypotensive AHF), which is associated with poor prognosis, particularly when hypoperfusion is also present.[17]

Table 2: Classification and Common Clinical Characteristics of Patients with AHF

CLINICAL CLASSIFICATION	SYMPTOM ONSET	TRIGGERS	SIGNS AND SYMPTOMS
Decompensated Heart Failure	Usually gradual	Non compliance, ischemia, infections	Peripheral oedema, Orthopnoea, Dyspnoea on exertion
Acute Hypertensive Heart Failure	Usually sudden	Hypertension, atrial arrhythmias, ACS	Dyspnoea, tachypnea, tachycardia, rales
Cardiogenic Shock	variable	Progressed of advanced HF or myocardial insult	End organ hypo perfusion, oliguria, confusion, cold extremities

Clinical classification can be based on bedside physical examination in order to detect the presence of clinical symptoms/signs of congestion ('wet' vs. 'dry' if present vs. absent) and/or peripheral hypoperfusion ('cold' vs. 'warm' if present vs. absent)[17] This classification may be helpful to guide therapy in the initial phase and carries prognostic information.[17]

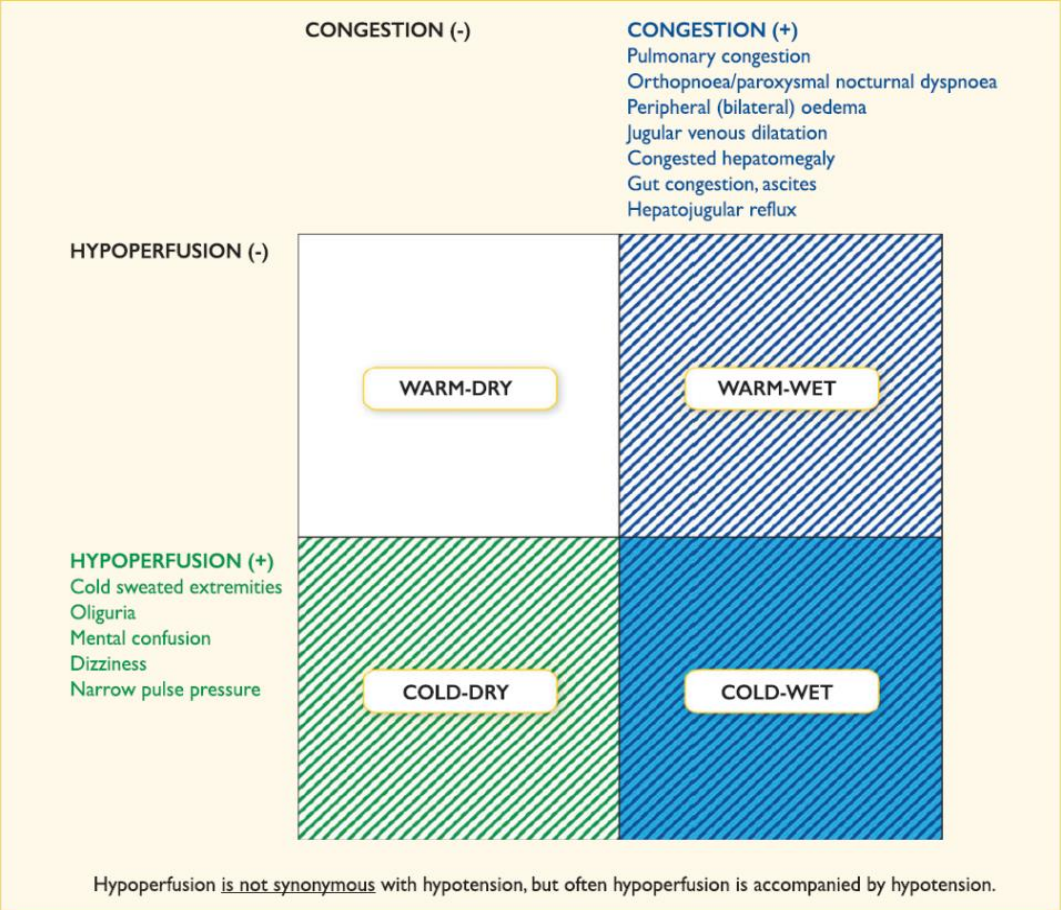


Figure 4: Clinical profiles of patients with acute heart failure based on presence/absence of congestion and/or hypo perfusion

Patients with HF complicating AMI can be classified according to **Killip and Kimball** [18]

Class I: no clinical signs of HF;

Class II: HF with rales and S3 gallop;

Class III: with frank acute pulmonary oedema;

Class IV: cardiogenic shock, hypotension (SBP ,90 mmHg) and evidence of peripheral vasoconstriction such as oliguria, cyanosis and diaphoresis.

Table 3: Factors Triggering Acute Heart Failure

Acute coronary syndrome.
Tachyarrhythmia (e.g. atrial fibrillation, ventricular tachycardia).
Excessive rise in blood pressure.
Infection (e.g. pneumonia, infective endocarditis, sepsis).
Non-adherence with salt/fluid intake or medications.
Bradyarrhythmia.
Toxic substances (alcohol, recreational drugs).
Drugs (e.g. NSAIDs, corticosteroids, negative inotropic substances, cardiotoxic chemotherapeutics).
Exacerbation of chronic obstructive pulmonary disease.
Pulmonary embolism.
Surgery and perioperative complications.
Increased sympathetic drive, stress-related cardiomyopathy.
Metabolic/hormonal derangements (e.g. thyroid dysfunction, diabetic ketosis, adrenal dysfunction, pregnancy and peripartum related abnormalities).
Cerebrovascular insult.
Acute mechanical cause: myocardial rupture complicating ACS (free wall rupture, ventricular septal defect, acute mitral regurgitation), chest trauma or cardiac intervention, acute native or prosthetic valve incompetence secondary to endocarditis, aortic dissection or thrombosis.

EPIDEMIOLOGY, AETIOLOGY AND NATURAL HISTORY OF HEART FAILURE

The prevalence of HF depends on definition applied, but is approximately 1–2% of the adult population in developed countries, rising to ≥10% among people >70 years of age.[19] The life time risk of HF at age 55 years is 33% for men and 28%for women.[20] The proportion of patients with HFpEF ranges from 22to73%, depending on age and sex population.[21] Data on temporal trends based on hospitalized patients suggest that the incidence of HF may be decreasing, more for HFrEF than for HFpEF.[22] HFpEF and HFrEF have different epidemiological and aetiological profiles.

Compared with HFrEF, patients with HFpEF are older, more often women and more commonly have a history of hypertension and atrial fibrillation (AF), while a history of myocardial infarction is less common.[23] The characteristics of patients with HFmrEF are between those with HFrEF and HFpEF,[24] but further studies are needed to better characterize this population. Many patients will have several different pathologies—cardiovascular and non-cardiovascular—that conspire to cause HF.

Table 4: ETIOLOGIES OF HEART FAILURE[25]

Depressed Ejection Fraction (<40%) • Coronary artery disease- Myocardial infarction/ischemia • Chronic pressure overload- Hypertension, Obstructive valvular disease • Chronic volume overload- regurgitant valvular disease, intracardiac/extracardiac shunting • Chronic lung disease- cor pulmonale, pulmonary vascular disorders • Non ischemic dilated cardiomyopathies • Toxic/drug induced damage • Chagas disease • Disorders of rate and rhythm-bradyarythmias, tachyarthmias
Preserved ejection fraction (≥50) • Pathologic hypertrophy-hypertrophic cardiomyopathy/ Hypertension • Aging • Restrictive cardiomyopathies- infiltrative/ storage disorders • Endomyocardial fibrosis
High output states • Metabolic disorders • Thyrotoxicosis • Nutritional deficiencies • Excessive blood flow requirements-systemic arteriovenous fistula, chronic anemia

PATHOPHYSIOLOGY OF HEART FAILURE[25]

Heart failure begins after an index event produces an initial decline in the heart's pumping capacity. After this initial decline in pumping capacity, a variety of compensatory mechanisms are activated, including the adrenergic nervous system, the renin-angiotensin-aldosterone system, and the cytokine system. 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. However, with time the sustained activation of these systems can lead to secondary end-organ damage within the ventricle, with worsening left ventricular remodeling and subsequent cardiac decompensation

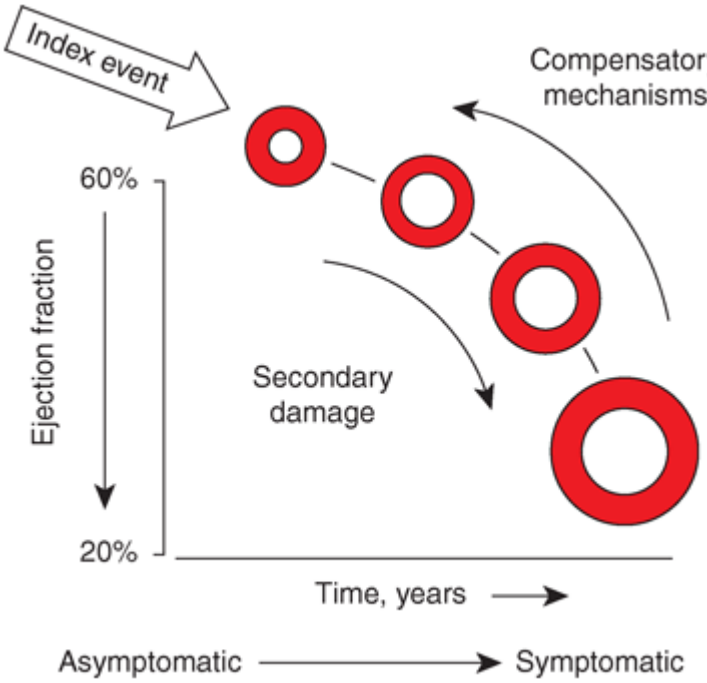


Figure 5: Pathogenesis of heart failure with a depressed ejection fraction

The decreased cardiac output in HF patients results in an "unloading" of high-pressure baroceptors (circles) in the left ventricle, carotid sinus, and aortic arch. This unloading of the peripheral baroreceptors leads to a loss of inhibitory parasympathetic tone to the central nervous system, with a resultant generalized increase in efferent sympathetic tone, and non-

osmotic release of arginine vasopressin (AVP) from the pituitary. AVP is a powerful vasoconstrictor that increases the permeability of the renal collecting ducts, leading to the reabsorption of free water. These afferent signals to the CNS also activate efferent sympathetic nervous system pathways that innervate the heart, kidney, peripheral vasculature, and skeletal muscles.

Sympathetic stimulation of the kidney leads to the release of renin, with a resultant increase in the circulating levels of angiotensin II and aldosterone. The activation of the renin-angiotensin-aldosterone system promotes salt and water retention and leads to vasoconstriction of the peripheral vasculature, myocyte hypertrophy, myocyte cell death, and myocardial fibrosis. Although these neurohormonal mechanisms facilitate short-term adaptation by maintaining blood pressure, and hence perfusion to vital organs, the same neurohormonal mechanisms are believed to contribute to end-organ changes in the heart and the circulation and to the excessive salt and water retention in advanced HF

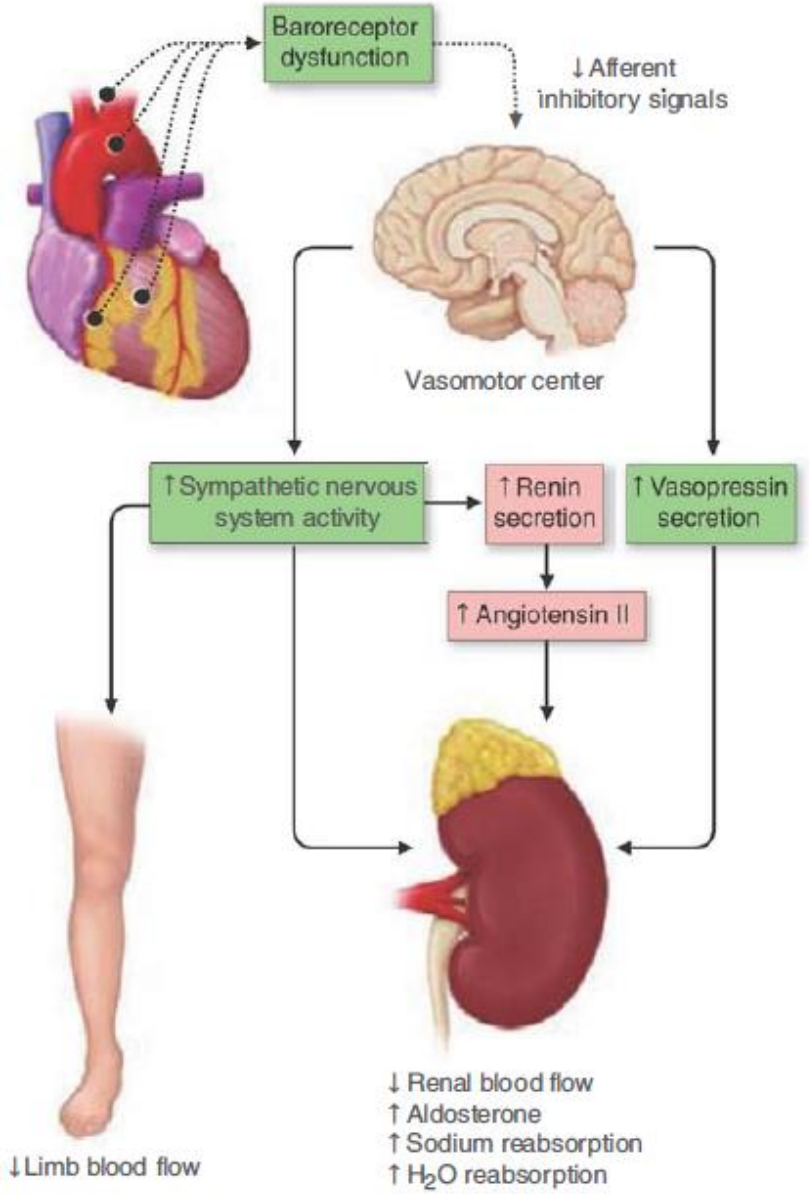


Figure 6: Activation of neurohormonal systems in heart failure.

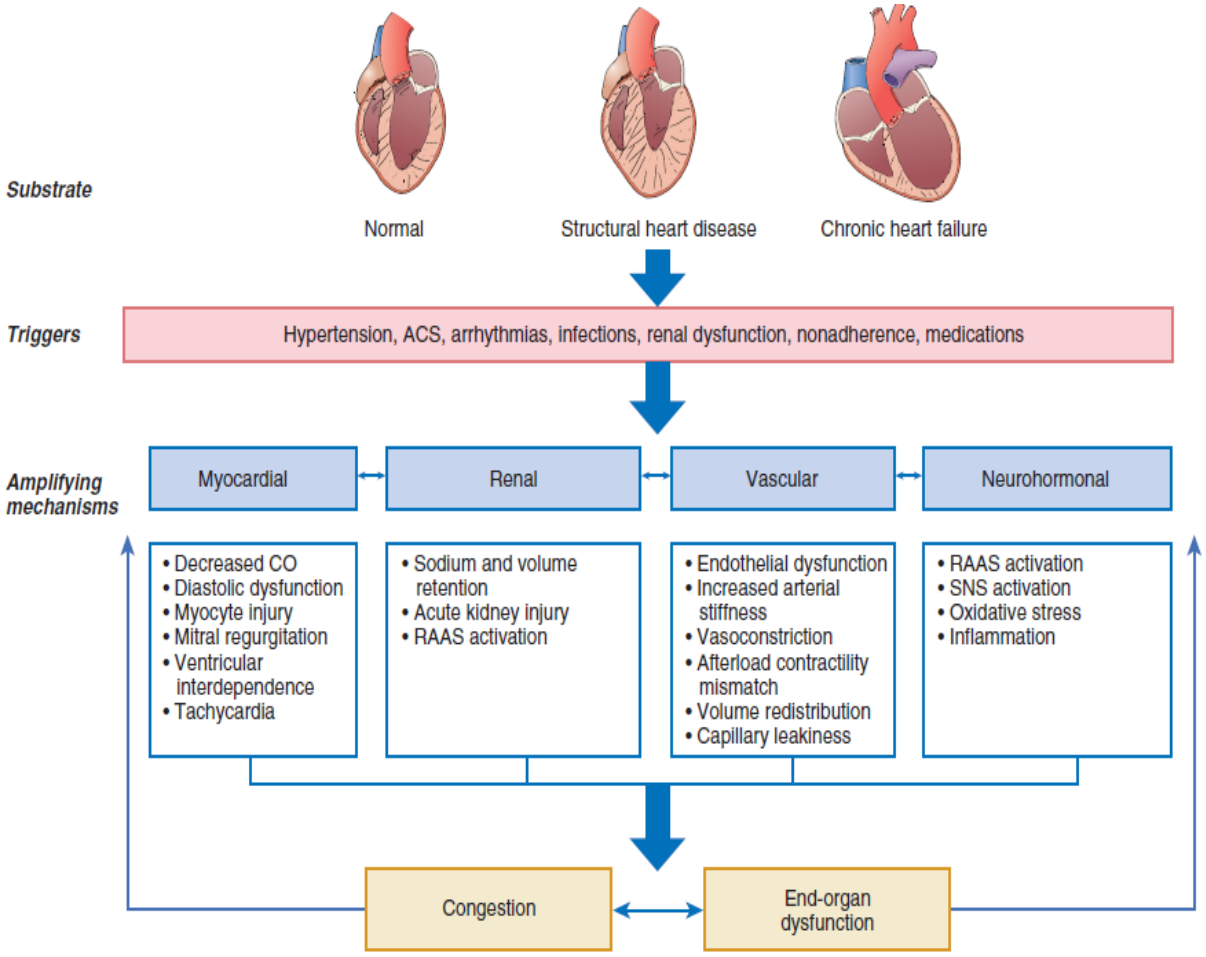


Figure 7: A schematic representation of the pathophysiology of AHF.

ACS = acute coronary syndrome; CO = cardiac output; RAAS = renin-angiotensin-aldosterone system; SNS = sympathetic nervous system.

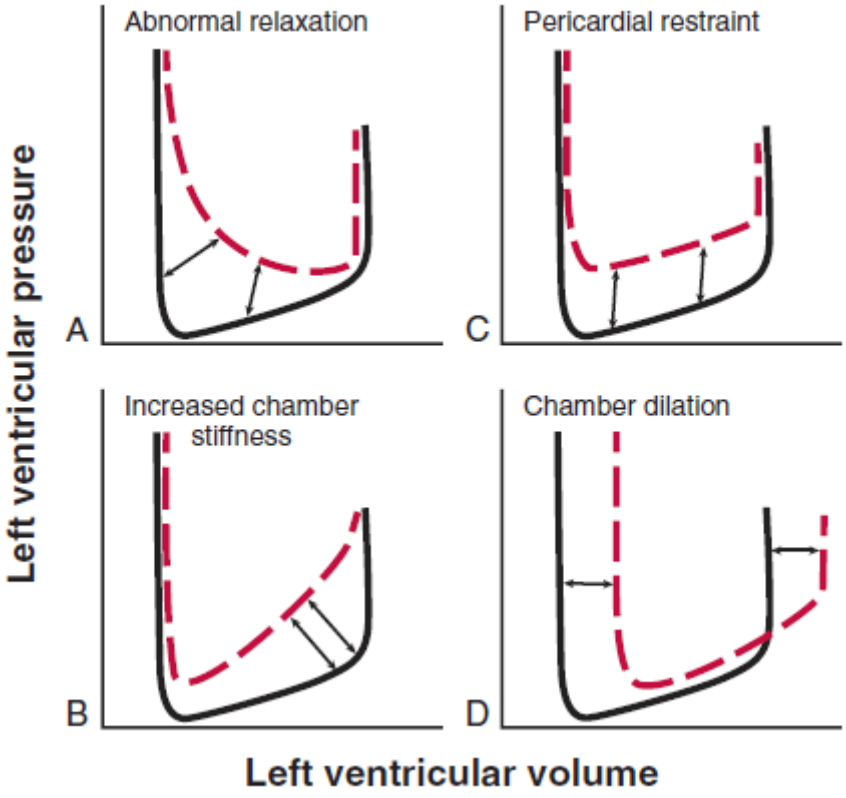


Figure 8: Mechanisms that result in increased LV diastolic pressure.

Among patients with heart failure and an increased LV diastolic pressure, four patterns of DPVR (Determinants of Pressure Volume Relationship) can be discerned. DPVR in patients with HFpEF may be characterized by graphed curves A to C. In the most prevalent pattern in HFpEF, represented by curve B, the DPVR is shifted upward and to the left, indicating reduced distensibility, where LV pressure is increased at any LV volume. In patients with HFpEF, when relaxation is markedly prolonged and diastole is abbreviated, as shown in curve A, LV diastolic pressure falls throughout diastole but remains increased. In curve C, pericardial constraint causes a parallel upward shift in the DPVR. DPVR in patients with HFrEF typically is characterized by curve D, in which eccentric remodelling results in a shift of the DPVR to the right, representing an increase in distensibility. It should be recognized that although the ventricle is more distensible, the end diastolic volume in these patients typically is very large and the end-diastolic stiffness in the operating region is high.[26]

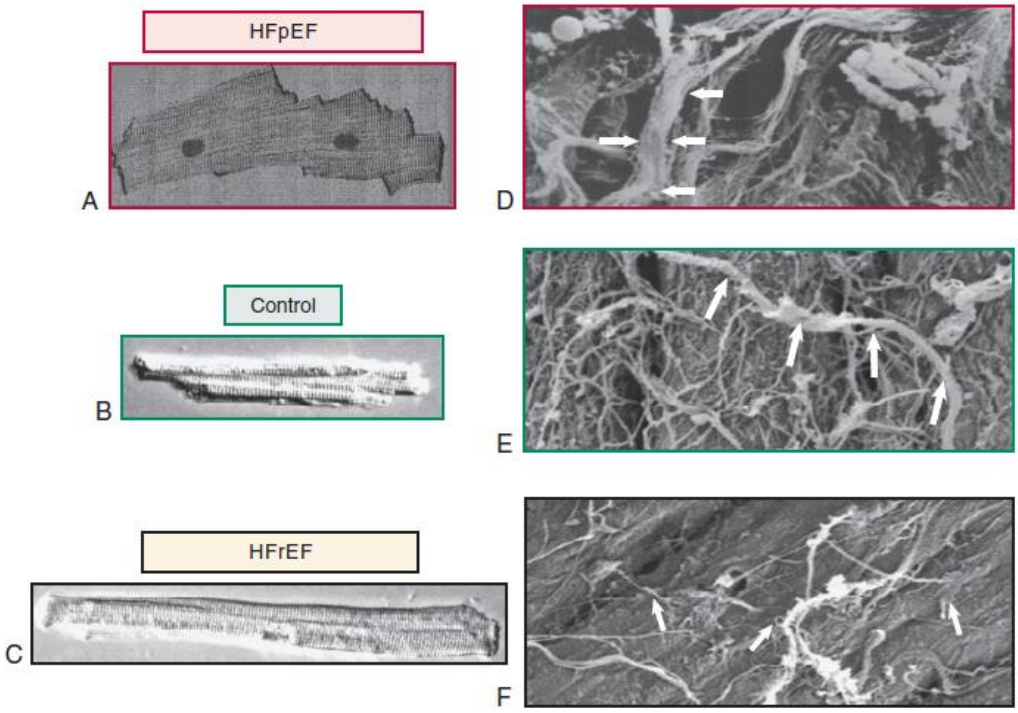


Figure 9: Changes in cardiomyocyte structure (A-C) and extracellular matrix fibrillar collagen (D-F) in HFpEF (outlined in red) versus HFrEF (outlined in black) versus findings in referent control group (outlined in green). Arrows indicate fibrillar collagen.

HFpEF is associated with concentric cardiomyocyte remodelling with increased diameter but no change in length and increased fibrillar collagen content, thickness, and number. By contrast, HFrEF is associated with eccentric cardiomyocyte remodelling with increased length but no change in width and fibrillar collagen degradation and abnormal structure and turnover.[26]

CLINICAL FEATURES

SYMPTOMS AND SIGNS

Symptoms are often non-specific and do not, therefore, help discriminate between HF and other problems.[27]

Symptoms and signs of HF due to fluid retention may resolve quickly with diuretic therapy. Signs, such as elevated jugular venous pressure and displacement of the apical impulse, may be more specific, but are harder to detect and have poor reproducibility.[28]

Symptoms and signs may be particularly difficult to identify and interpret in obese individuals, in the elderly and in patients with chronic lung disease.[29]

Younger patients with HF often have a different aetiology, clinical presentation and outcome compared with older patients.[30]

Table 5: Physical Signs in Heart Failure

Physical findings in heart failure
Tachycardia
Extra beats and irregular rhythm
Narrow pulse pressure or thready pulse
Pulsus alternans
Tachypnea
Cooled and/or mottled extremities
Elevated jugular venous pressure
Dullness or diminished breath sounds at one or both lung bases
Rales, rhonchi, and or wheezes
Apical impulse sustained, shifted leftward and /or inferiorly
Parasternal lift
S3 and S4 heart sounds
Tricuspid and mitral regurgitation murmur
Hepatomegaly
Ascites
Chronic venous stasis changes

ESSENTIAL INVESTIGATIONS

Table 6: LEVEL OF EVIDENCE[31] (ESC 2016 GUIDELINES)

Level of evidence A	**Data derived from multiple randomized clinical trials or meta-analyses.**
Level of evidence B	**Data derived from a single randomized clinical trial or large non-randomized studies.**
Level of evidence C	**Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.**

Table 7: CLASSES OF RECOMMENDATION[31] (ESC 2016 GUIDELINES)

Classes of recommendations	Definition	Suggested wording to use
Class I	**Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.**	**Is recommended/is indicated**
Class II	**Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.**	
Class IIa	***Weight of evidence/opinion is in favour of usefulness/efficacy.***	**Should be considered**
Class IIb	***Usefulness/efficacy is less well established by evidence/opinion.***	**May be considered**
Class III	**Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.**	**Is not recommended**

Table 8: RECOMMENDATIONS OF NECESSARY INVESTIGATIONS

Recommendations	Class [a]	Level [b]
The following diagnostic tests are recommended/should be considered for initial assessment of a patient with newly diagnosed HF in order to evaluate the patient's suitability for particular therapies, to detect reversible/treatable causes of HF and co-morbidities interfering with HF:		
- haemoglobin and WBC - sodium, potassium, urea, creatinine (with estimated GFR) - liver function tests (bilirubin, AST, ALT, GGTP) - glucose, HbA1c - lipid profile - TSH - ferritin, TSAT = TIBC	I	C
- natriuretic peptides	IIa	C
Additional diagnostic tests aiming to identify other HF aetiologies and comorbidities should be considered in individual patients with HF when there is a clinical suspicion of a particular pathology (see Table 3.4 on HF aetiologies).	IIa	C
A 12-lead ECG is recommended in all patients with HF in order to determine heart rhythm, heart rate, QRS morphology, and QRS duration, and to detect other relevant abnormalities. This information is needed to plan and monitor treatment.	I	C
Exercise testing in patients with HF:		
- is recommended as a part of the evaluation for heart transplantation and/or mechanical circulatory support (cardiopulmonary exercise testing);	I	C
- should be considered to optimize prescription of exercise training (preferably cardiopulmonary exercise testing);	IIa	C
- should be considered to identify the cause of unexplained dyspnoea (cardiopulmonary exercise testing).	IIa	C
- may be considered to detect reversible myocardial ischaemia.	IIb	C
Chest radiography (X-ray) is recommended in patients with HF to detect/exclude alternative pulmonary or other diseases, which may contribute to dyspnoea. It may also identify pulmonary congestion/oedema and is more useful in patients with suspected HF in the acute setting.	I	C
Right heart catheterization with a pulmonary artery catheter:		
- is recommended in patients with severe HF being evaluated for heart transplantation or mechanical circulatory support;	I	C
- should be considered in patients with probable pulmonary hypertension assessed by echocardiography in order to confirm pulmonary hypertension and its reversibility before the correction of valve/structural heart disease;	IIa	C
- may be considered in order to adjust therapy in patients with HF who remain severely symptomatic despite initial standard therapies and whose haemodynamic status is unclear.	IIb	C
EMB should be considered in patients with rapidly progressive HF despite standard therapy when there is a probability of a specific diagnosis which can be confirmed only in myocardial samples and specific therapy is available and effective.	IIa	C
Thoracic ultrasound may be considered for the confirmation of pulmonary congestion and pleural effusion in patients with AHF.	IIb	C
Ultrasound measurement of inferior vena cava diameter may be considered for the assessment of volaemia status in patients with HF.	IIb	C

NATRIURETIC PEPTIDES (NP)

Patients with normal plasma NP concentrations are unlikely to have HF.

The upper limit of normal in the non-acute setting for B-type natriuretic peptide (BNP) is 35 pg/mL and for N-terminal pro-BNP (NT-proBNP) it is 125 pg/Ml. In the acute setting, higher values should be used [BNP , 100 pg/mL, NT-proBNP , 300 pg/ mL and mid-regional pro A-type natriuretic peptide (MR-proANP) , 120 pmol/L].

Diagnostic values apply similarly to HFrEF and HFpEF; on average, values are lower for HFpEF than for HFrEF.[32]

At the mentioned exclusionary cut-points, the negative predictive values are very similar and high (0.94–0.98) in both the non-acute and acute setting, but the positive predictive values are lower both in the non-acute setting (0.44–0.57) and in the acute setting (0.66–0.67).[33] Therefore, the use of NPs is recommended for ruling-out HF, but not to establish the diagnosis.

There are numerous cardiovascular and non-cardiovascular causes of elevated NPs that may weaken their diagnostic utility in HF. Among them, AF, age and renal failure are the most important factors impeding the interpretation of NP measurements.[34]

On the other hand, NP levels may be disproportionally low in obese patients.[35]

ELECTROCARDIOGRAM

An abnormal electrocardiogram (ECG) increases the likelihood of the diagnosis of HF, but has low specificity.[36]

ECG provide information on aetiology (e.g. myocardial infarction), and findings on the ECG might provide indications for therapy (e.g. anticoagulation for AF, pacing for bradycardia, CRT if broadened QRS complex).

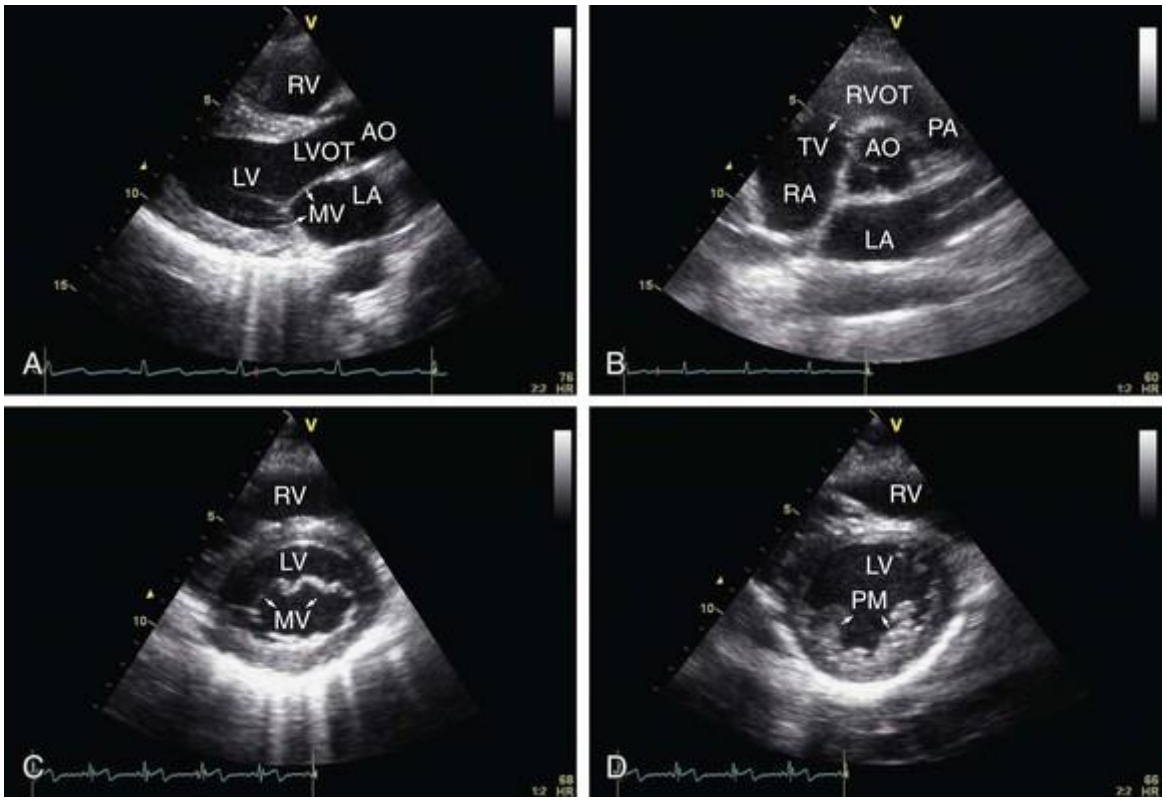
HF is unlikely in patients presenting with a completely normal ECG (sensitivity 89%).[37]Therefore, the routine use of an ECG is mainly recommended to rule out HF.

CARDIAC IMAGING AND OTHER DIAGNOSTIC TESTS

Cardiac imaging plays a central role in the diagnosis of HF and in guiding treatment. Echocardiography is the method of choice in patients with suspected HF, for reasons of accuracy, availability (including portability) safety and cost.[38]

TRANSTHORACIC ECHOCARDIOGRAPHY

Echocardiography is a term used here to refer to all cardiac ultrasound imaging techniques, including two-dimensional/three-dimensional echocardiography, pulsed and continuous wave Doppler, colour flow Doppler, tissue Doppler imaging (TDI) contrast echocardiography and deformation imaging (strain and strain rate). Transthoracic echocardiography (TTE) is the method of choice for assessment of myocardial systolic and diastolic function of both left and right ventricles.



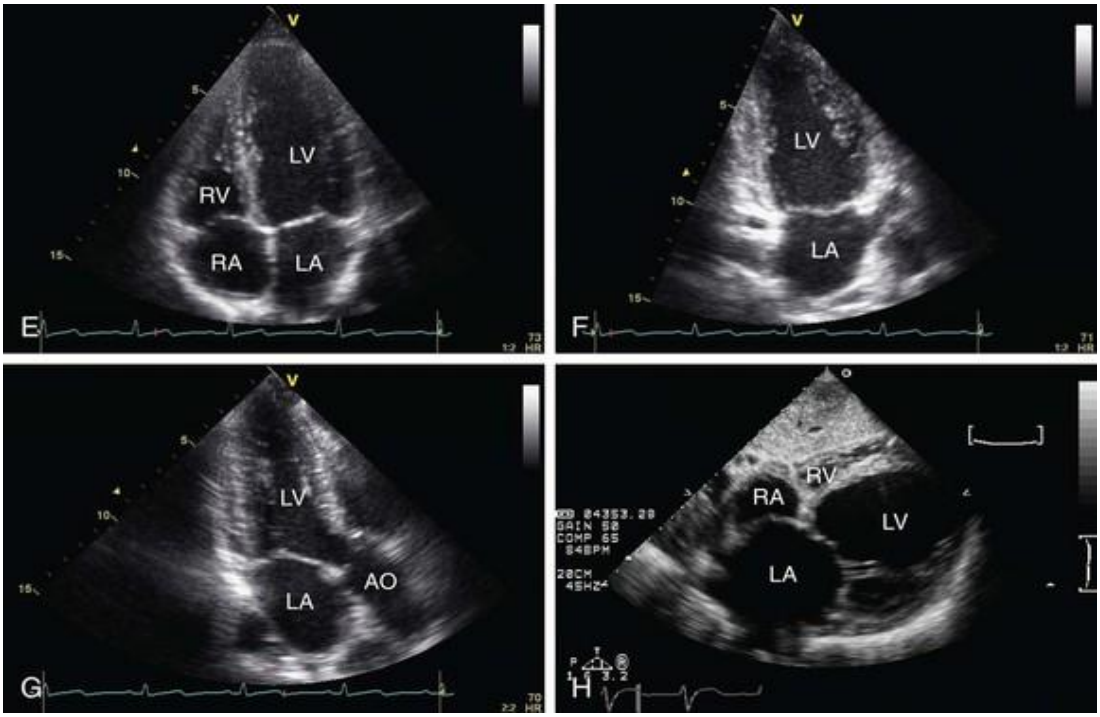


Figure 10: Basic plane views for transthoracic echocardiography: A through **D**: Parasternal position. **A**, long axis view. **B**, short axis view, aortic valve level. **C**, short axis view of basal left ventricle with opened mitral valve. **D**, short axis view of left ventricle, at papillary muscles level (mid left ventricle). **E**, **F,** and **G**: apical view images. **E**, apical four-chamber view. **F**, two-chamber view. **G**, three-chamber view. **H**, subcostal view. AO, aorta; ASC Ao, ascending aorta; DESC Ao, descending aorta; LV, left ventricle; LVOT, LV outflow tract; MV, mitral valve; PA, pulmonary artery; PM, papillary muscles; RV, right ventricle; RVOT, RV outflow tract; TV, tricuspid valve.

ASSESSMENT OF LEFT VENTRICULAR SYSTOLIC FUNCTION

For measurement of LVEF, the modified biplane Simpson's rule is recommended. LV end diastolic volume (LVEDV) and LV end systolic volume (LVESV) are obtained from apical four- and two-chamber views. This method relies on accurate tracing of endocardial borders.[39] Measurement of regional wall motion abnormalities is relevant for patients suspected of CAD or myocarditis.

ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION

Although echocardiography is at present the only imaging technique that can allow for the diagnosis of diastolic dysfunction, no single echocardiography variable is sufficiently accurate to be used in isolation to make a diagnosis of LV diastolic dysfunction.

Key structural alterations are a left atrial volume index (LAVI) >34 mL/m2 or a left ventricular mass index (LVMI) ≥115 g/m2 for males and ≥95 g/m2 for females.[40]Key functional alterations are E/e′ ≥13 and a mean e'septal and lateral wall < 9 cm/s.[41]

Other(indirect) echocardiographically derived measurements are longitudinal strain or tricuspid regurgitation velocity (TRV).[42]

CHEST X-RAY

The chest X-ray may, show pulmonary venous congestion or oedema in a patient with HF, and is more helpful in the acute setting than in the non-acute setting.[43]

Significant LV dysfunction may be present without cardiomegaly on the chest X-ray.[43]

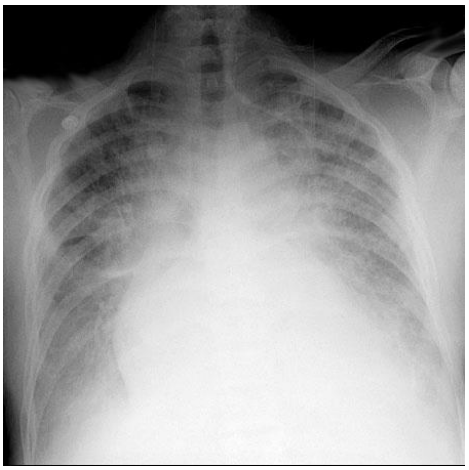


Figure 11: This is a typical chest-x-ray of a patient in severe CHF, showing cardiomegaly, alveolar oedema, and haziness of vascular margins

TRANSOESOPHAGEAL ECHOCARDIOGRAPHY

Transoesophageal echocardiography (TOE) is not needed in the routine diagnostic assessment of HF;

It may be valuable in patients with suspected valve disease, aortic dissection, endocarditis or congenital heart disease and for ruling out intra cavitary thrombi in AF patients requiring cardioversion.

STRESS ECHOCARDIOGRAPHY

Exercise or pharmacological stress echocardiography may be used for the assessment of inducible ischaemia and/or myocardium viability and in some clinical scenarios of patients with valve disease (e.g. dynamic mitral regurgitation, low-flow–low-gradient aortic stenosis).[44]

It allow the detection of diastolic dysfunction related to exercise exposure in patients with exertional dyspnoea, preserved LVEF and inconclusive diastolic parameters at rest.[45]

CARDIAC MAGNETIC RESONANCE(CMR)

CMR is the gold standard for the measurements of volumes, mass and EF of both the left and right ventricles.

It is the best alternative cardiac imaging modality for patients with non-diagnostic echocardiographic studies (particularly for imaging of the right heart) and is the method of choice in patients with complex congenital heart diseases.[46]

CORONARY ANGIOGRAPHY

Coronary angiography is recommended in patients with HF who suffer from angina pectoris recalcitrant to medical therapy, in patients with a history of symptomatic ventricular arrhythmia or aborted cardiac arrest.[47]

DIAGNOSIS OF HEART FAILURE

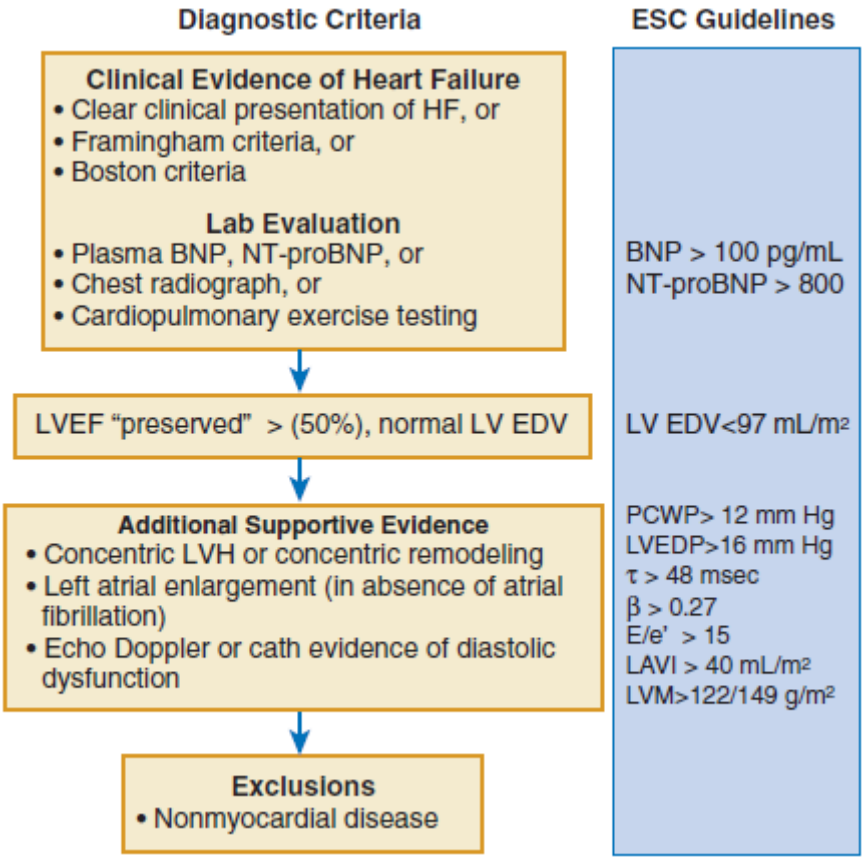


Figure 12: Diagnostic criteria for HFpEF from the Heart Failure Society of America (HFSA) (left) and the European Society of Cardiology (ESC) (right) guidelines.

EDV = end-diastolic volume; LAVI = left atrial volume index; LVEDP = left ventricular end diastolic pressure; LVM = left ventricular mass (index for female/male); PCWP = pulmonary capillary wedge pressure

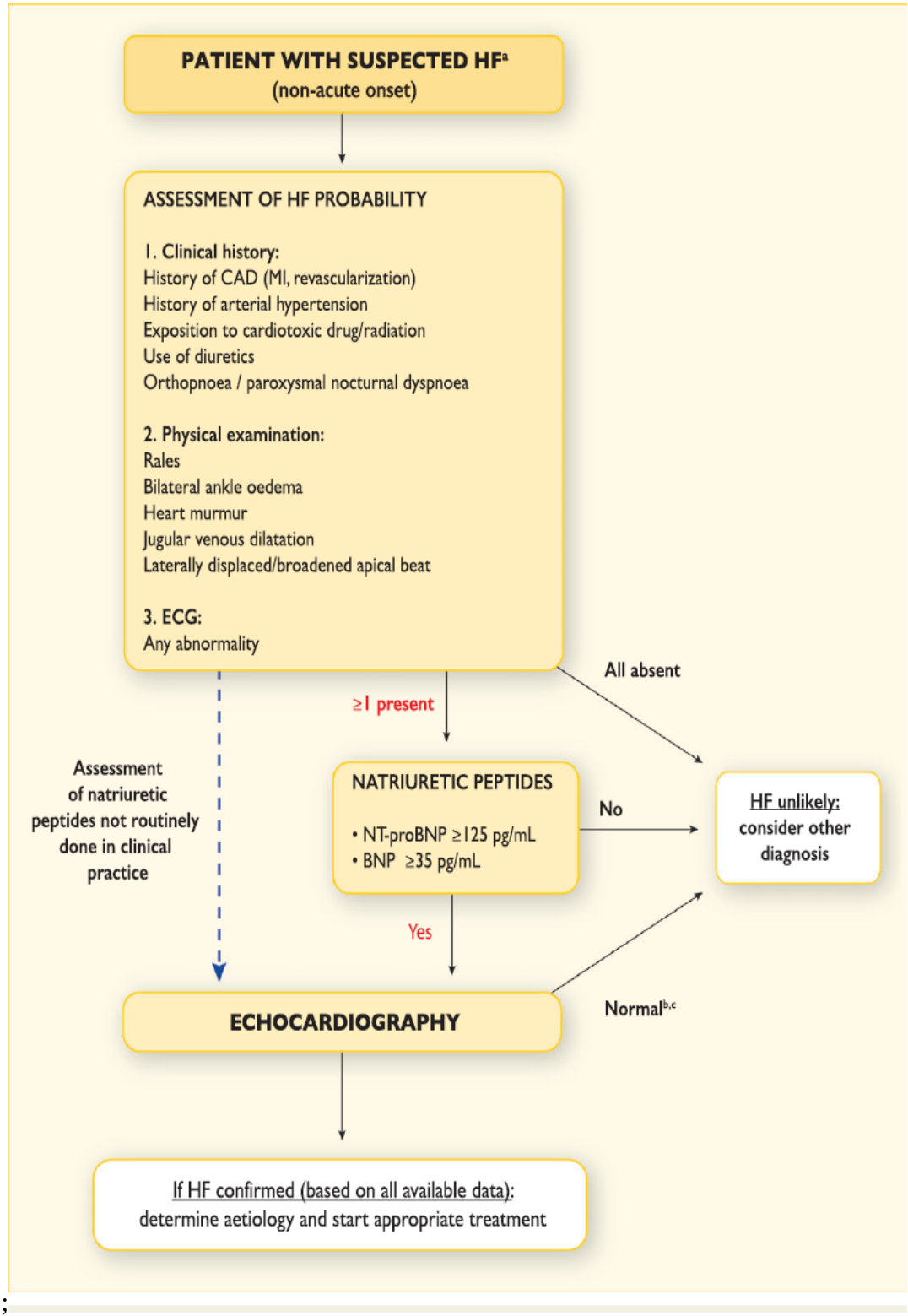


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Figure 13: Algorithm for a diagnosis of heart failure of non-acute onset.

a:Patient reporting symptoms typical of HF. b: Normal ventricular and atrial volumes and function. c: other causes of elevated natriuretic peptides to be considered.

HEART FAILURE AND CO-MORBIDITIES

Co-morbidities are of great importance in HF and may affect the use of treatments for HF (e.g.it may not be possible to use renin–angiotensin system inhibitors is some patients with severe renal dysfunction). The drugs used to treat comorbidities may cause worsening of HF (e.g.NSAIDs given for arthritis, some anti-cancer drugs). HFpEF has an even higher prevalence of co-morbidities compared with HFrEF, and many of these may be instrumental in the progression of this syndrome.[48]

DIABETES MELLITUS

- Dysglycaemia and diabetes are very common in HF, and diabetes is associated with poorer functional status and worse prognosis. In patients with HFrEF, interventions that reduce morbidity and mortality confer similar benefit in the presence or absence of diabetes.[49] Whether strict glycaemic control alters the risk of cardiovascular events in patients with HF is uncertain.[50]
- Among patients with HF higher HbA1c is associated with greater risk of cardiovascular events,[51] In patients with diabetes and HF, glycaemic control should be implemented gradually and moderately, giving preference to those drugs, such as metformin, that have been shown to be safe and effective.
- Metformin is safe to use in patients with HFrEF, and it should be the treatment of choice in patients with HF but is contraindicated in patients with severe renal or hepatic impairment, because of the risk of lactic acidosis.[50]
- Insulin is required for patients with type 1 diabetes and to treat symptomatic hyperglycaemia in patients with type 2 diabetes and pancreatic islet b cell exhaustion. However, insulin is a powerful sodium-retaining hormone, and when combined with a reduction in glycosuria, may exacerbate fluid retention, leading to HF worsening.

- Sulphonyl urea derivatives have also been associated with an increased risk of worsening HF and should be used with caution. Thiazolidinediones (glitazones) cause sodium and water retention and increased risk of worsening HF and hospitalization and are not recommended in patients with HF.[52]
- Dipeptidylpeptidase-4 inhibitors (DPP4I; gliptins), improve glycaemic indices but do not reduce and may increase the risk of cardiovascular events and worsening HF.[49] There are no data on the safety of gliptins and GLP-1 analogues in patients with HF. Recently, empagliflozin, an inhibitor of sodium-glucose co transporter 2, reduced hospitalization for HF and mortality.[53]As glycaemic derangement progresses, the judgement on glycaemic control should be made according to cardiac conditions.

HYPERTENSION

- Hypertension is associated with an increased risk of developing HF; antihypertensive therapy markedly reduces the incidence of HF (with an exception of a-adrenoceptor blockers, which are less effective than other antihypertensives in preventing HF).[54]
- A recent prospective cohort study documented that in a population with incident HF, higher baseline systolic, diastolic and pulse pressure levels were associated with a higher rate of adverse events, which further supports the importance for optimized blood pressure control in this population.[55]
- Negatively inotropic CCBs (i.e. diltiazem and verapamil) should not be used to treat hypertension in patients with HFrEF (but are believed to be safe in HFpEF), and moxonidine should also be avoided in patients with HFrEF, as it increased mortality in patients in one RCT.[56]

- If blood pressure is not controlled with an ACEI (or an ARB), a beta-blocker, an MRA and a diuretic, then hydralazine and amlodipine[57] [or felodipin[58]] are additional blood pressure lowering agents that have been shown to be safe in systolic HF.
- In patients with AHF intravenous nitrates (or sodium nitroprusside) are recommended to lower blood pressure.[59]

ANGINA AND CORONARY ARTERY DISEASE

- Beta-blockers, and in selected patients ivabradine,[60] are effective agents for angina control, as well as an essential component of HFrEF therapy. In HFpEF patients, they may also be used for angina relief.[61]
- Trimetazidine has been shown to exert some beneficial effect as an add-on to beta-blockers in patients with HF and angina.[62] There are data suggesting that it may improve NYHA functional capacity, exercise duration and LV function in patients with HFrEF.[63]
- The safety of other anti-anginal agents in HFrEF, such as ranolazine, is uncertain, while other drugs, specifically diltiazem and verapamil, are thought to be unsafe in patients with HFrEF (although they may be used in HFpEF).[64]
- Dihydropyridine CCBs may all increase sympathetic tone, and their safety in HFrEF [except amlodipine[57] and felodipine[58]] and HFpEF is uncertain.[64]

HYPERLIPIDAEMIA

- Elevated low-density lipoprotein cholesterol is uncommon in HFrEF; patients with advanced HFrEF often have low concentrations of low-density lipoprotein, which is associated with a worse prognosis.

- Rosuvastatin did not reduce the primary composite mortality/ morbidity endpoints in two large RCTs in patients with HF with or without IHD, but it also did not increase risk, and may have reduced, hospitalizations.[65]
- There is no evidence to recommend the initiation of statins in most patients with HF.

HYPOKALAEMIA AND HYPERKALAEMIA

- Both hypokalaemia and hyperkalaemia are associated with HF and with many drugs used for HF treatment.[66] Both can aggravate ventricular arrhythmias.
- Loop and thiazide diuretics reduce serum potassium, while ACEIs, ARBs and MRAs can all increase serum potassium. Amiloride and triamterene are used as adjunct diuretics in resistant oedema and to assist in preventing hypokalaemia.
- The treatment of hypokalaemia can involve recommending high potassium foods or prescribing potassium supplements.
- The management of acute hyperkalaemia (.6.0 mmol/L) may require a short-term cessation of potassium-retaining agents and RAAS inhibitors. A Cochrane review[67] found no trial evidence of major outcome benefits for any emergency therapy regimen for hyperkalaemia.
- Two new potassium binders (patiromer and sodium zirconium cyclosilicate) are currently under consideration for regulatory approval.[68]

IRON DEFICIENCY AND ANAEMIA

- Iron deficiency is common in HF, as it is with other chronic illnesses, and it can lead to anaemia and/or skeletal muscle dysfunction without anaemia.[69]Within an HF population, iron deficiency is associated with a worse prognosis.[70]

- Anaemia (defined as a haemoglobin concentration ,13.0 g/dL in men and ,12.0 g/dL in women) is common in HF, particularly in hospitalized patients. It is more common in women, the elderly and in patients with renal impairment and is associated with advanced myocardial remodelling, inflammation and volume overload.[71]
- Anaemia is associated with advanced symptoms, worse functional status, greater risk of HF hospitalization and reduced survival.
- The erythropoietin-stimulating agent darbepoetin alfa did not improve clinical outcomes in HFrEF patients with mild to moderate anaemia, but led to an excess of thromboembolic events and is therefore not recommended.[72]

LUNG DISEASES (ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE)

- The diagnosis of COPD and asthma may be difficult in patients with HF, due to overlap in symptoms and signs,but also problems in the interpretation of spirometry, especially in HFpEF. COPD (and asthma) in patients with HF may be overdiagnosed.[73]
- Beta-blockers are only relatively contraindicated in asthma, but not in COPD, although a more selective b1-adrenoceptorantagonist (i.e. bisoprolol, metoprolol succinate, or nebivolol) is preferred.[73]
- Oral corticosteroids can cause sodium and water retention, potentially leading to worsening of HF
- Pulmonary hypertension can complicate severe long-standing COPD, which, as a result, makes right-sided HF and congestion more likely.

- Non-invasive ventilation, added to conventional therapy, improves the outcome of patients with acute respiratory failure due to hypercapnic exacerbation of COPD or HF in situations of acute pulmonary oedema.[73]

KIDNEY DYSFUNCTION (CHRONIC KIDNEY DISEASE, ACUTE KIDNEY INJURY, CARDIO-RENAL SYNDROME AND PROSTATIC OBSTRUCTION)

- HF and CKD frequently coexist, share many risk factors (diabetes, hypertension, hyperlipidaemia) and interact to worsen prognosis.[74]
- Deterioration in renal function, termed worsening renal function (WRF), is used to indicate an increase in serum creatinine, usually by >26.5 mmol/L (0.3 mg/dL) and/or a 25% increase or a 20% drop in GFR.
- WRF is relatively common, especially during initiation and up titration of RAAS inhibitor therapy.
- Patients with HF and coronary or peripheral vascular disease are at risk of acute renal dysfunction when they undergo contrast media enhanced angiography [contrast-induced acute kidney injury (CI-AKI)].
- Prostatic obstruction is common in older men and can interfere with renal function; it should therefore be ruled out in men with HF with deteriorating renal function. Alpha-adrenoceptor blockers cause hypotension and sodium and water retention, and may not be safe in HFrEF.[75] Hence, 5-a-reductase inhibitors are generally preferred in the medical treatment of prostatic obstruction in patients with HF.

OBESITY

- Obesity is a risk factor for HF[76] and complicates its diagnosis, because it can cause dyspnoea, exercise intolerance and ankle swelling and may result in poor-quality echocardiographic images.

- Obese individuals also have reduced NP levels.[77] Obesity is more common in HFpEF than in HFrEF,
- Although obesity is an independent risk factor for developing HF, once HF is diagnosed, it is well established that obesity is associated with lower mortality across a wide range of body mass indexes (BMIs) —the so-called **obesity paradox** also seen in other chronic illnesses.[78]
- When weight loss is occurring in HF, it is associated with high mortality and morbidity, worse symptom status and poor quality of life.[79]
- In patients with HF with moderate degrees of obesity (BMI ,35 kg/m2), weight loss cannot be recommended.
- In more advanced obesity (BMI 35–45 kg/m2), weight loss may be considered to manage symptoms and exercise capacity.[80]

SLEEP DISTURBANCE AND SLEEP-DISORDERED BREATHING

- Sleep-disordered breathing(SDB)occurs in more than one-third of patients with HF being even more prevalent in patients with AHF.[81]
- The most common types are: central sleep apnoea (CSA, similar to Cheyne Stokes respiration, CSR), obstructive sleep apnoea (OSA), and a mixed pattern of the two.
- Other causes of sleep disturbance include anxiety, depression, decubitus or paroxysmal pulmonary congestion (orthopnoea and paroxysmal nocturnal dyspnoea) and diuretic therapy causing nocturnal diuresis.
- CSA and OSA have been shown to be associated with a worse prognosis in HF.[81]
- OSA is associated with an increased risk of incident HF in men.[82]
- CSA is the most common form of SDB in HFrEF, and HFrEF is the most common cause of CSA, so they are closely linked.

- Nocturnal oxygen supplementation, continuous positive airway pressure(CPAP), bi-level positive airway pressure(BiPAP), and adaptive servo-ventilation (ASV) may be considered to treat nocturnal hypoxaemia in OSA.[83]
- CPAP in HF related CSA has been shown to reduce the frequency of episodes of apnoea and hypopnoea, and improve LVEF and 6-minute walk test distance, but did not improve prognosis or the rate of HF related hospitalizations.[84]

CACHEXIA AND SARCOPENIA

- Cachexia is a generalized wasting process affecting all body compartments [i.e. lean tissue (skeletal muscle), fat tissue (energy reserves) and bone tissue (osteoporosis)].
- It may occur in 5–15% of patients with HF, especially those with HFrEF, and more advanced disease status.[85]
- Cachexia in HF can be diagnosed and defined as involuntary non-oedematous weight loss ≥6% of total body weight with in the previous 6–12months.[86]
- The causes are multifactorial, and may include pro-inflammatory immune activation, neurohormonal derangements, poor nutrition and malabsorption, impaired calorie and protein balance, anabolic hormone resistance, reduced anabolic drive, prolonged immobilization and physical deconditioning, together characterized by catabolic/anabolic imbalance.[87]
- Skeletal muscle wasting, when associated with impaired mobility and symptoms (termed sarcopenia or myopenia), occurs in 30–50% of patients with HFrEF.[88]
- In its most severe form it is associated with frailty and poor morbidity and mortality. Potential treatments may include appetite stimulants, exercise training and anabolic agents, including testosterone, in combination with the application of nutritional

supplements and anti-catabolic interventions, although none is of proven benefit and their safety is unknown.[89]

CENTRAL NERVOUS SYSTEM (DEPRESSION, STROKE AND AUTONOMIC DYSFUNCTION)

- Stroke and HF commonly coexist because of an overlap of shared risk factors. Both contribute to a worse prognosis. Autonomic dysfunction is common in HFrEF, especially when severe.[90]
- Depression is common and is associated with worse clinical status and a poor prognosis in HF.
- Selective serotonin re up take inhibitors are thought to be safe, although the Sertraline Antidepressant Heart Attack Randomized Trial did not confirm that sertraline provides a greater reduction in depressive symptoms or improvement in cardiovascular status compared with placebo in HFrEF patients.
- Tricyclic antidepressants should be avoided, because they may cause hypotension, worsening HF and arrhythmias.[91]

DELAYING OR PREVENTING THE DEVELOPMENT OF OVERT HEART FAILURE

Table 9: Recommendations to prevent or delay the development of overt heart failure or prevent death before the onset of symptoms

Recommendations	Class [a]	Level [b]
Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A
Treatment with statins is recommended in patients with or at high-risk of CAD whether or not they have LV systolic dysfunction, in order to prevent or delay the onset of HF and prolong life.	I	A
Counselling and treatment for smoking cessation and alcohol intake reduction is recommended for people who smoke or who consume excess alcohol in order to prevent or delay the onset of HF.	I	C
Treating other risk factors of HF (e.g. obesity, dysglycaemia) should be considered in order to prevent or delay the onset of HF.	IIa	C
Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life.	IIa	B
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF.	I	B
ACE-I should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, in order to prevent or delay the onset of HF.	IIa	A
Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF or prolong life.	I	B
ICD is recommended in patients: a) with asymptomatic LV systolic dysfunction (LVEF ≤30%) of ischaemic origin, who are at least 40 days after acute myocardial infarction, b) with asymptomatic non-ischaemic dilated cardiomyopathy (LVEF ≤30%), who receive OMT therapy, in order to prevent sudden death and prolong life.	I	B

ACEI-angiotensin-converting enzyme inhibitor; CAD-coronary artery disease; HF-heart failure; ICD-implantable cardioverter-defibrillator; LV-left ventricular; LVEF-left ventricular ejection fraction; OMT-optimal medical therapy

- Many trials show that control of hypertension will delay the onset of HF and some also show that it will prolong life.[92]
- Different antihypertensive drugs [diuretics, ACEIs, angiotensin receptor blockers (ARBs), beta-blockers] have been shown to be effective, especially in older people, both in patients with and without a history of myocardial infarction.[92]
- The recent SPRINT study has already demonstrated that treating hypertension to a lower goal [systolic blood pressure (SBP) ,120 mmHg vs.,140 mmHg] in older hypertensive subjects (≥75 years of age) or high-risk hypertensive patients reduces the risk of cardiovascular disease, death and hospitalization for HF.[93]
- Recently, empaglifozin (an inhibitor of sodium-glucose cotransporter2), has been shown to improve outcomes (including the reduction of mortality and HF hospitalizations) in patients with type 2 diabetes.[94] Other hypoglycaemic agents have not been shown convincingly to reduce the risk of cardiovascular events and may increase the risk of HF. Although smoking cessation has not been shown to reduce the risk of developing HF.[95]
- The association between alcohol intake and the risk of developing de novo HF is U-shaped, with the lowest risk with modest alcohol consumption (up to 7 drinks/week).[96]Greater alcohol intake may trigger the development of toxic cardiomyopathy, and when present, complete abstention from alcohol is recommended.
- An inverse relationship between physical activity and the risk of HF has been reported.[97]

- Statins reduce the rate of cardiovascular events and mortality; there is also reasonable evidence that they prevent or delay the onset of HF.[98] Neither aspirin nor other antiplatelet agents, nor revascularization, have been shown to reduce the risk of developing HF or mortality in patients with stable CAD.
- Obesity is also a risk factor for HF but the impact of treatments of obesity on the development of HF is unknown.

MANAGEMENT OF HEART FAILURE

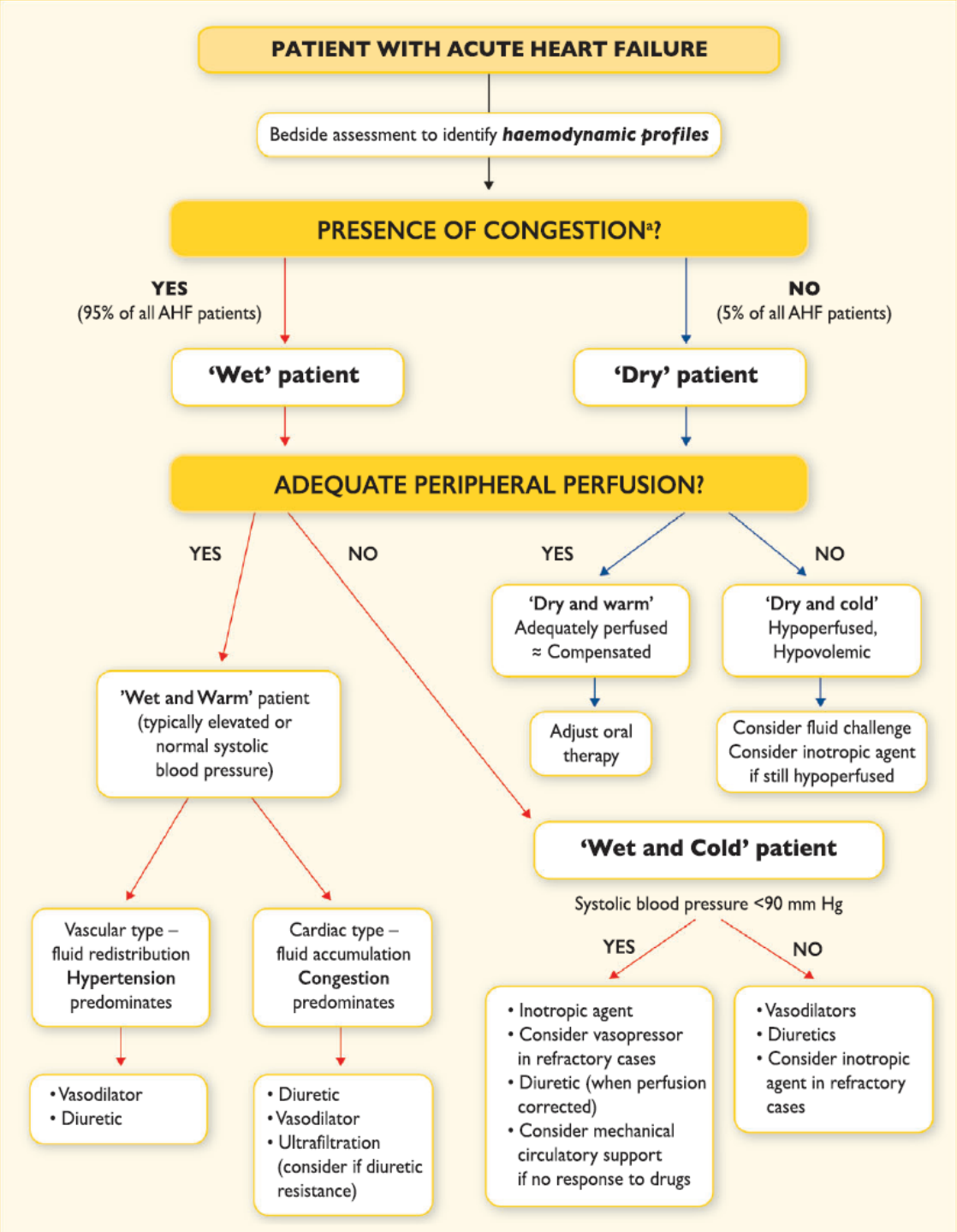


Figure 14; Management of patients with acute heart failure based on clinical profile during an early phase. a: **Symptoms/signs of congestion**

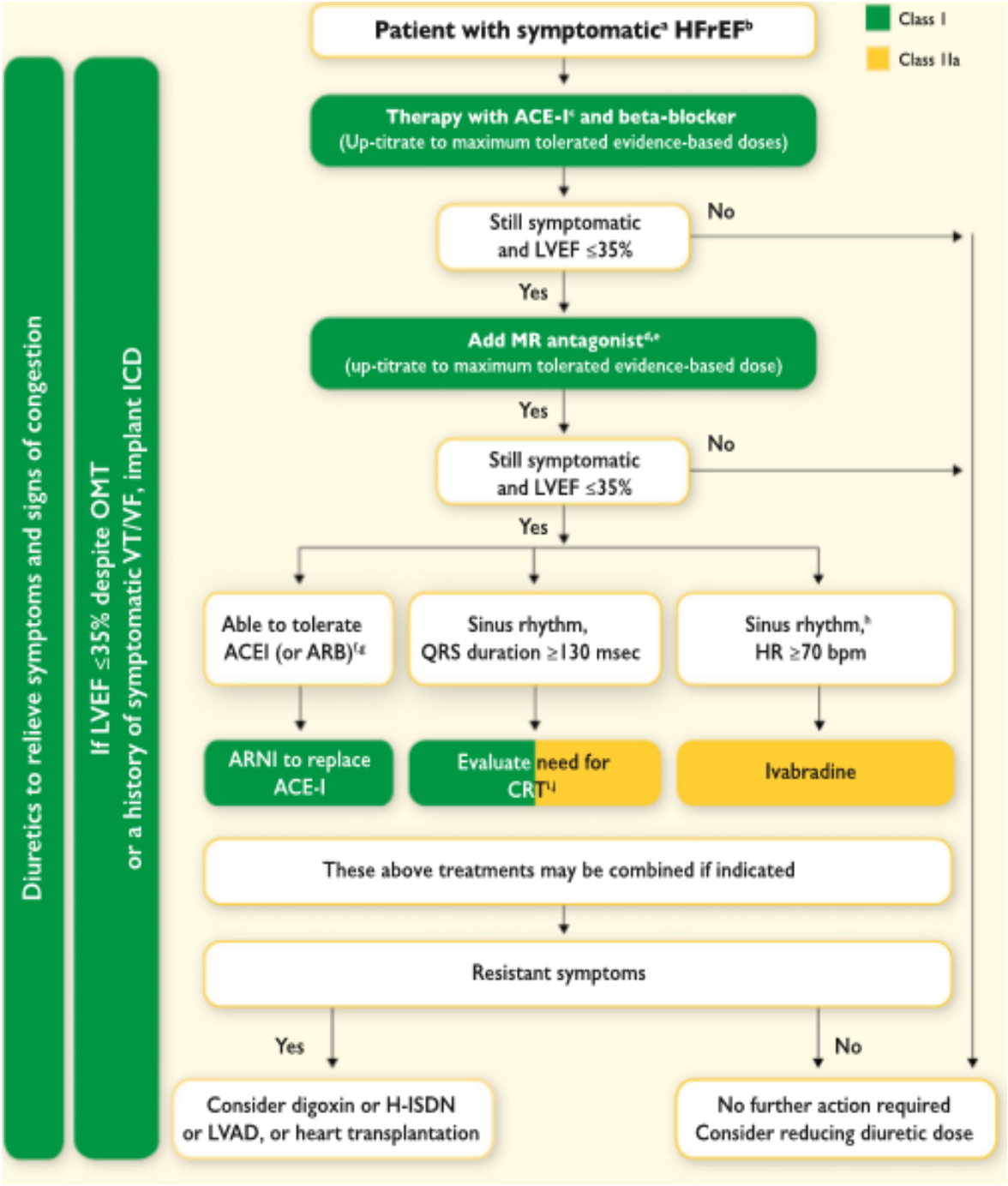


Figure 15: Therapeutic algorithm for a patient with symptomatic heart failure with reduced ejection fraction. Green indicates class I recommendation; yellow indicates a class IIa recommendation.

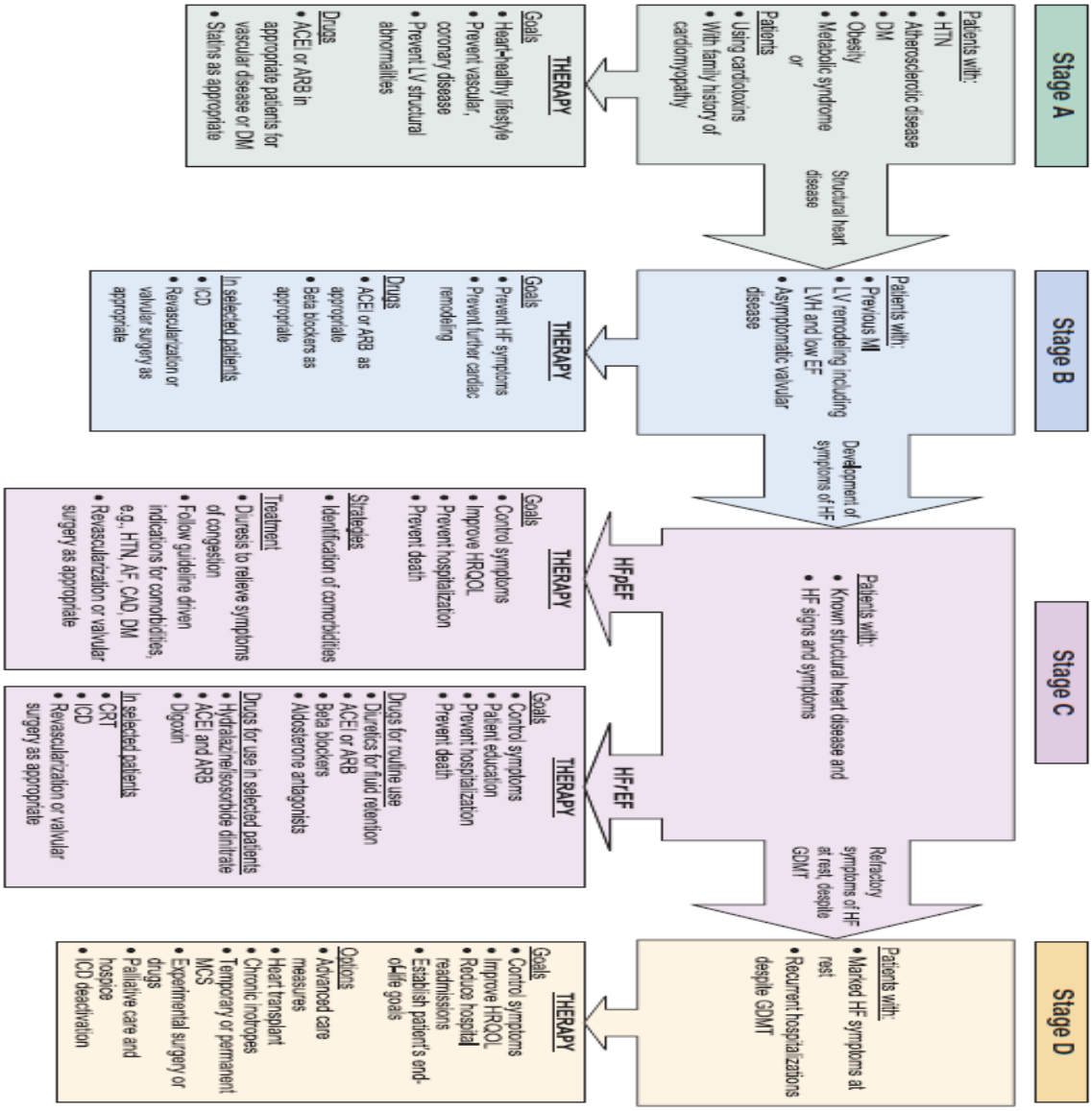


Figure 16: Stages in the development of HF and recommended therapy by stage.

MORTALITY AND MORBIDITY

The most recent European data (ESC-HF pilot study) demonstrate that 12-month all-cause mortality rates for hospitalized and stable/ambulatory HF patients were 17% and 7%, respectively, and the 12-month hospitalization rates were 44% and 32%, respectively.[99] In patients with HF (both hospitalized and ambulatory), most deaths are due to cardiovascular causes, mainly sudden death and worsening HF. All-cause mortality is generally higher in HFrEF than HFpEF.[100]Hospitalizations are often due to non-cardiovascular causes, particularly in patients with HFpEF. Hospitalization for cardiovascular causes did not change from 2000 to 2010, whereas those with non-cardiovascular causes increased.[101]

METHODOLOGY

SOURCE OF DATA: This is a prospective observational study. A total of 120 patients admitted to Patients admitted to Sri R.L.Jalappa Hospital and R L J H Narayana Heart Centre satisfying Framingham Criteria for diagnosis of heart failure were included in the study. Study was carried out from January 2015 to August 2016.

FRAMINGHAM CRITERIA FOR DIAGNOSIS OF HEART FAILURE

Major criteria:

1) Paroxysmal nocturnal dyspnoea
2) Jugular venous distention (or CVP>16 mmHg)
3) Rales or acute pulmonary oedema
4) Cardiomegaly
5) Hepatojugular reflex
6) Response to diuretic (weight loss>4.5 kg in 5 days)
7) S3 Gallop

Minor criteria:

1) Ankle oedema
2) Nocturnal cough
3) Exertional dyspnoea
4) Pleural effusion
5) Vital capacity<two thirds of normal
6) Hepatomegaly
7) Tachycardia(>120bpm)

Atleast two major or one major with two minor should be present to fulfil the diagnosis of heart failure.

Inclusion Criteria:

1) Patients aged more than 18 years
2) Patients fulfilling Framingham diagnostic criteria for heart failure

Exclusion Criteria:

1) Patients aged less than 18 years
2) Patients not fulfilling Framingham diagnostic criteria for heart failure

METHOD OF COLLECTION OF DATA

Patient's complete history was taken from the patient or patient's attendees and explained about the study and informed written consent was taken.

Patient was examined fully and appropriate investigations like Complete hemogram, Chest X ray-Postero Anterior view, Renal function tests, Serum electrolytes, Blood sugar level, thyroid profile, 12 Lead Electrocardiogram, Echocardiography (to confirm systolic and diastolic dysfunction) were done.

The World Health Organization defines anaemia as haemoglobin <13g% in males and <12g% in females.[102]

Blood Pressure grading according to JNC VII Classification [103]

Normal -	<120/80 mm of Hg
Prehypertension	120-139/80-89 mm of Hg
Stage 1 HTN	140-159/90-99 mm of Hg
Stage 2 HTN	≥160/≥ 100 mm of Hg
Isolated systolic HTN	>140/<90 mm of HG

2D ECHOCARDIOGRAPHY

The examination was performed while the patient was in a period of quiet respiration. All recordings performed included complete M-mode, 2-dimensional, and Doppler echocardiographic examinations, with emphasis on evaluation of LV diastolic and systolic function, LV size, and mass. Assessment of PV flow and E/A, E/e' during a valsalva maneuver were done when necessary. A minimum of 10 to 15 beats was recorded for all 2-dimensional, M-mode, and Doppler parameters. Apical 2, 3, and 4 chamber views were obtained in all echocardiographic studies.

Assessment of Left Ventricular diastolic function:

1) early filling peak velocity (E), 2) atrial filling peak velocity (A), 3) E/A ratio, 4) deceleration time (DT), 5) isovolumic relaxation time (IVRT) 6) E/A ratio during valsalva maneuver and 7) e'- Early diastolic myocardial velocities at mitral annulus 8)E/e' Left atrial volume index (LAVI) was calculated by the biplane area-length method from apical 2- and 4-chamber views indexed to body surface area.

Assessment of left ventricular systolic function:

For measurement of LVEF, the modified biplane Simpson's rule is recommended. LV end diastolic volume (LVEDV) and LV end systolic volume (LVESV) are obtained from apical four- and two-chamber views.

The Simpson method can be used to obtain LV volumes and then the calculated ejection fraction (EF) by the following formula.

Ejection Fraction = End Diastolic Volume (EDV)- End Systolic Volume (ESV)/EDV

Figure 17: Echocardiography in CCU

STATISTICAL ANALYSIS

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test of Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram and Scatter plots.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data. EPI Info (CDC Atlanta), Open Epi, Med calc and Medley's desktop were used to estimate sample size, odds ratio and reference management in the study.

RESULTS

Table 10: Age distribution of patients with Heart Failure

		Count	%
Age	< 50 years	21	17.9%
	51 to 75 years	74	61.2%
	> 75 years	25	20.9%
	Total	120	100.0%

Majority of patients were in the age group 51 to 75 years, 20.9% were >75 years and 17.9% were <50 years.

Chart 1: Pie diagram showing Age distribution of patients with Heart Failure

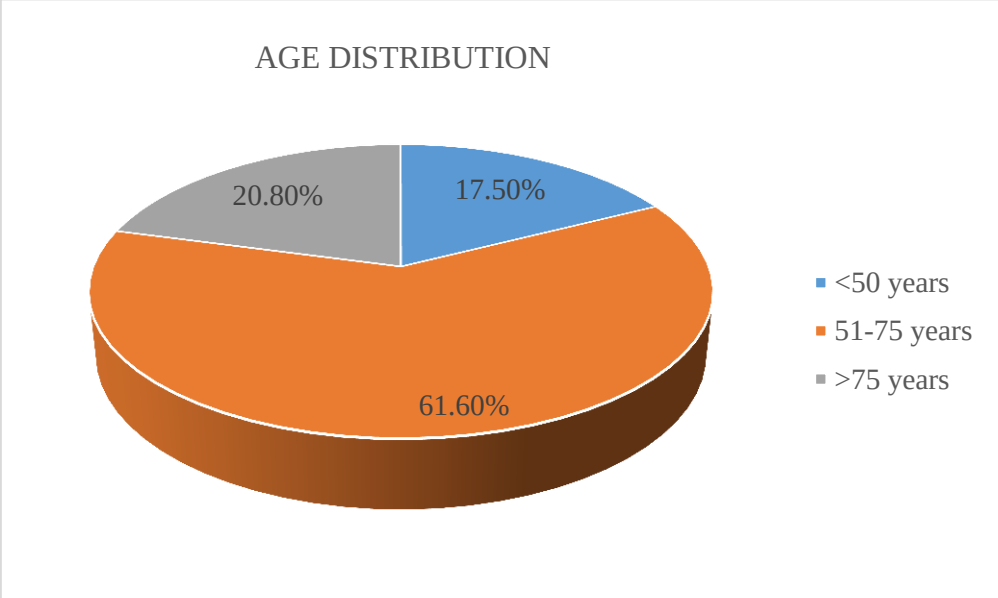


Table 11: Gender distribution among patients with Heart Failure

		Count	%
Sex	Male	69	57.5%
	Female	51	42.5%
	Total	120	100.0%

In the study majority of them were males (57.5%) and 42.5% were females.

Chart 2: Pie diagram showing gender distribution among patients with Heart Failure

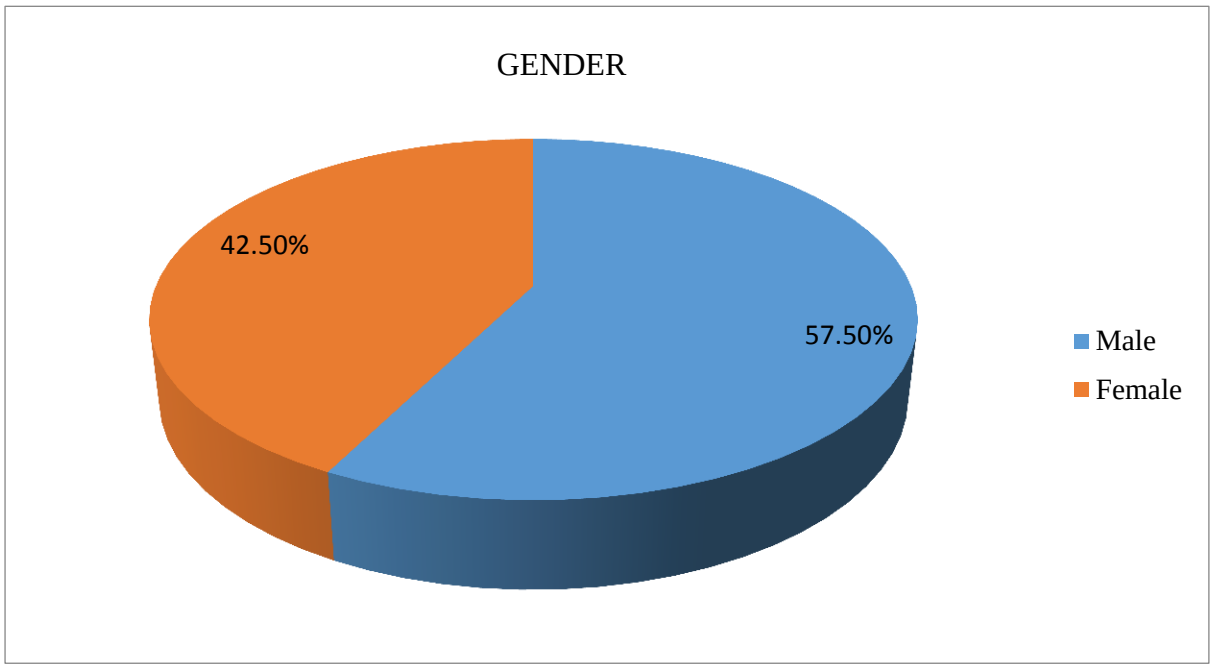


Table 12: Breathlessness grading(NYHA) among patients with Heart failure

		Count	%
Breathlessness	Grade I	17	14.2%
	Grade II	27	22.5%
	Grade III	41	34.2%
	Grade IV	32	26.7%
	No breathlessness	3	2.5%
	Total	120	100.0%

Majority of patients presented with Grade III breathlessness.

Chart 3 Bar diagram showing Breathlessness grading among patients with Heart failure

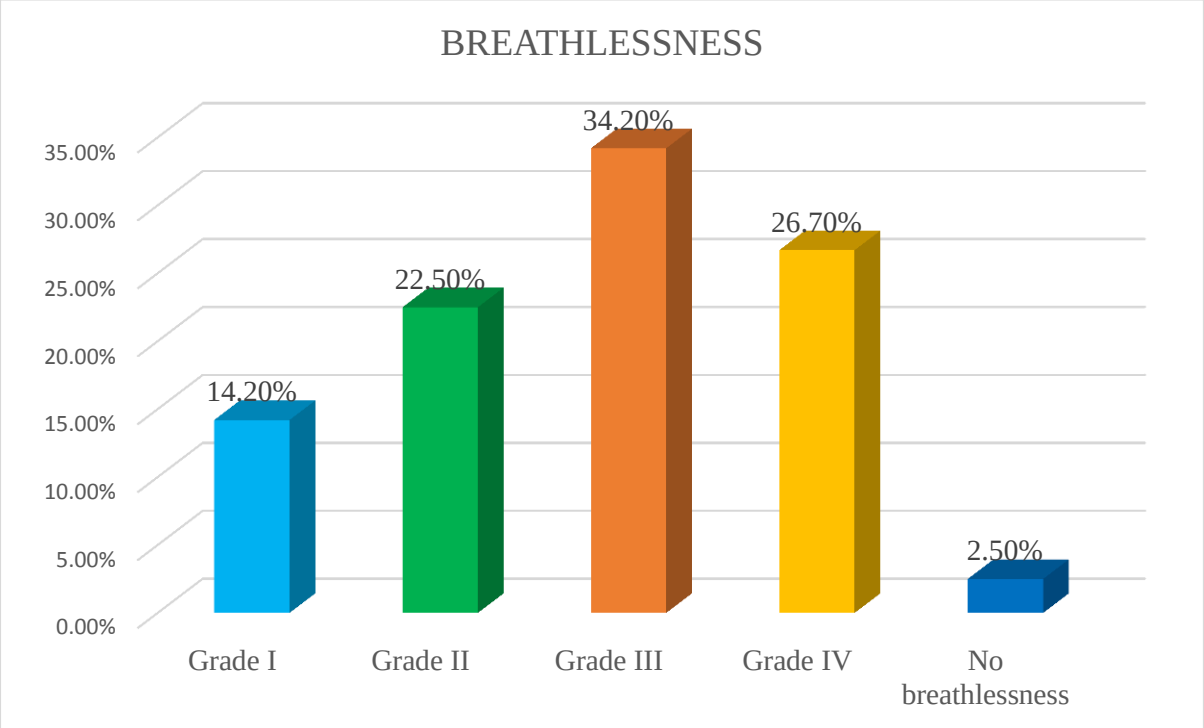


Table 13: Symptoms among patients with Heart Failure

	Present		Absent	
	Count	%	Count	%
Lower Limb Swelling	45	37.5%	75	62.5%
Cough	61	50.8%	59	49.2%
Palpitations	46	38.3%	74	61.7%
Chest Pain	50	41.7%	70	58.3%
Fever	32	26.7%	88	73.3%

*Multiple findings can be present for a patient

Most common symptom on presentation was cough (50.8%), followed by Chest pain (41.7%), palpitations (38.3%), lower limb swelling (37.5%) and fever (26.7%).

Chart 4: Bar diagram showing Symptoms among patients with Heart Failure

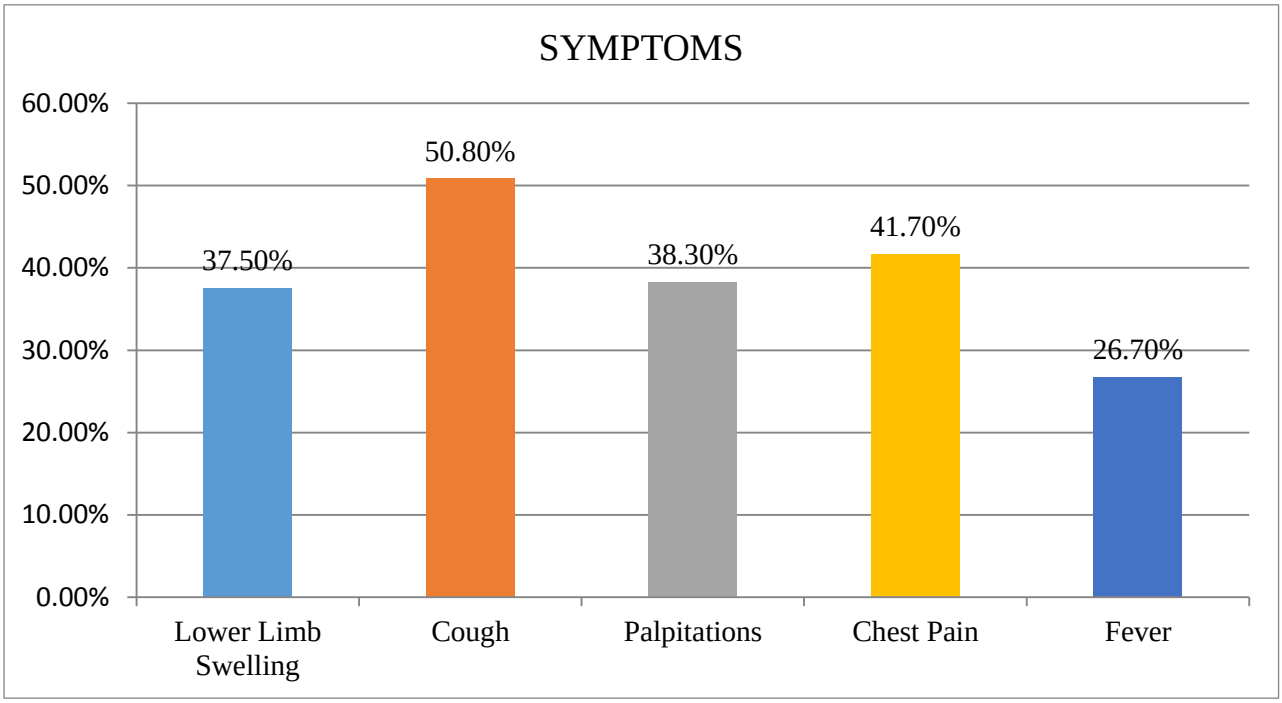


Table 14: Habits history among patients with Heart Failure

	Present		Absent	
	Count	%	Count	%
Smoking	41	34.2%	79	65.8%
Alcohol	36	30.0%	84	70.0%

In the study 34.2% were smokers and 30% were alcoholics.

Chart 5: Bar diagram showing Habits history among patients with Heart Failure

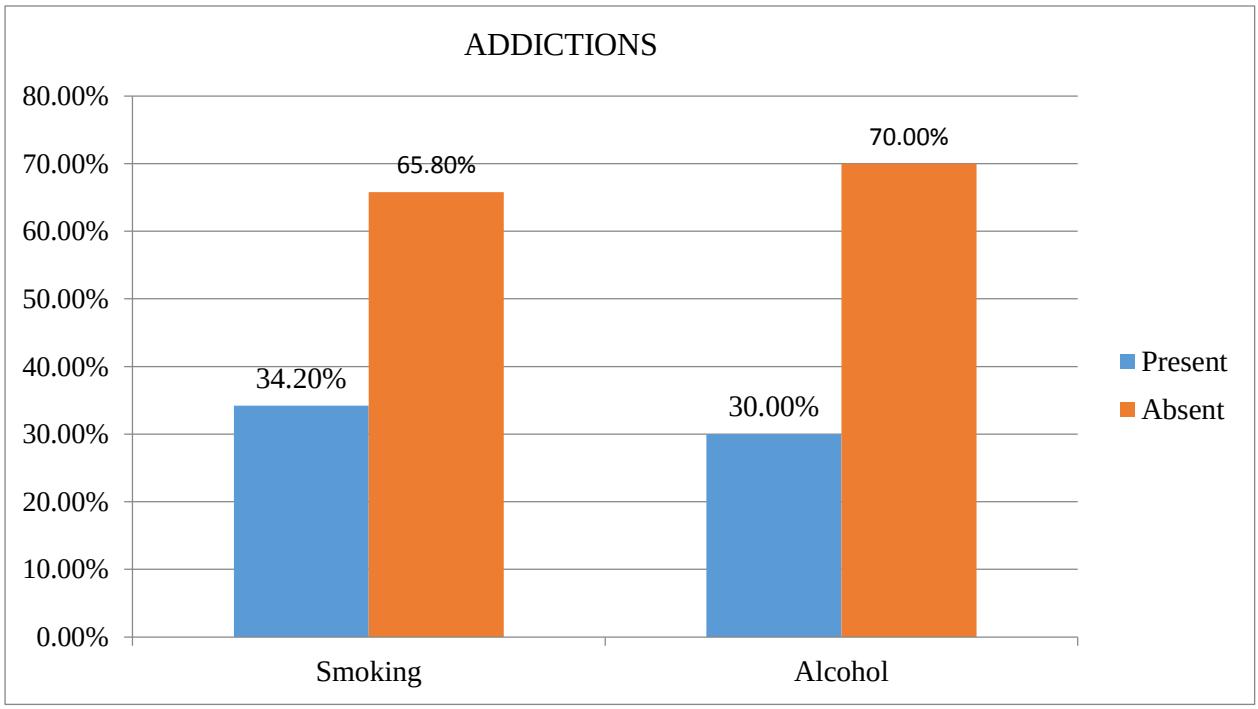


Table 15: Co morbidities among patients with Heart Failure

	Present		Absent	
	Count	%	Count	%
Hypertension	79	65.8%	41	34.2%
Coronary Artery Disease	67	55.8%	53	44.2%
Diabetes Mellitus	74	61.7%	46	38.3%
Atrial Fibrillation	25	20.8%	99	82.5%
COPD	41	34.2%	79	65.8%
Valvular heart diseases	12	10.0%	108	90.0%

*Multiple findings can be present for a patient

In the study 65.8% had HTN, 55.8% had CAD, 61.7% had diabetes mellitus, 20.8% had AF, 34.2% had COPD and 10% had valvular heart diseases.

Chart 6: Bar diagram showing Co morbidities among patients with Heart Failure

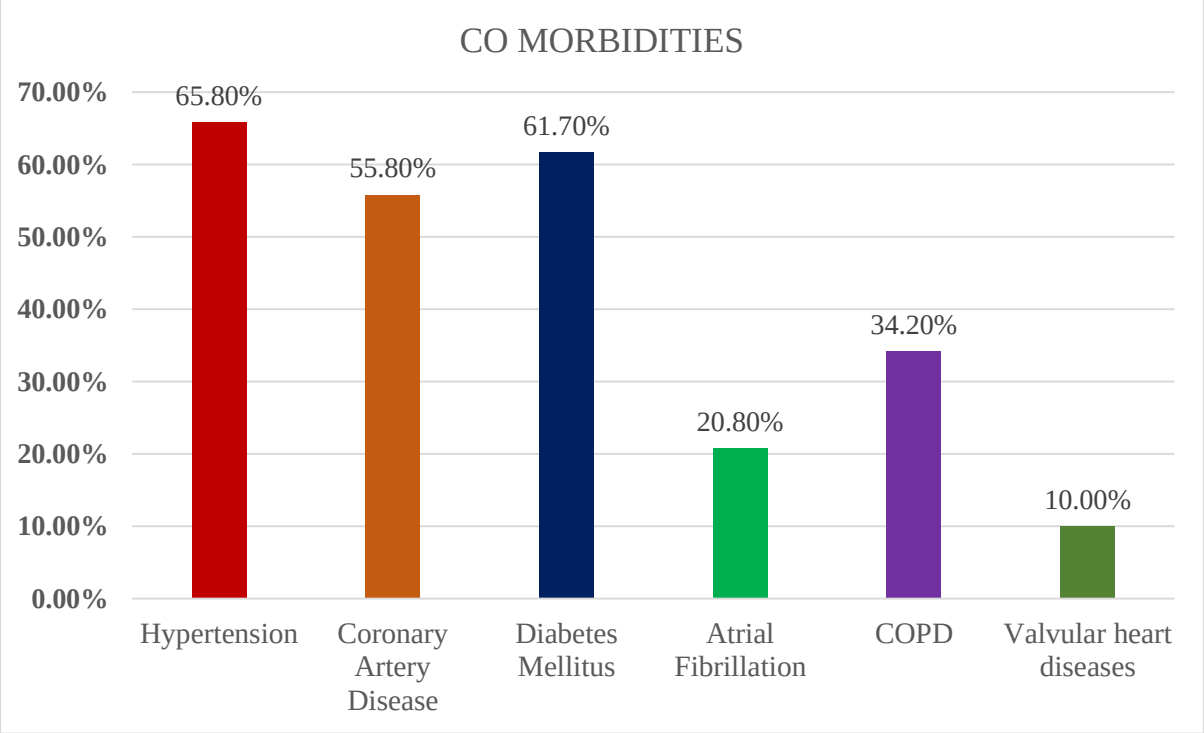


Table 16: Physical signs among patients with Heart Failure

	Present		Absent	
	Count	%	Count	%
Pallor	57	47.5%	63	52.5%
Icterus	0	0.0%	120	100.0%
Cyanosis	24	20.0%	96	80.0%
Clubbing	5	4.2%	115	95.8%
Edema	52	43.3%	68	56.7%
Raised JVP	52	43.3%	68	56.7%

*Multiple findings can be present for a patient

On examination it was observed that 47.5% had pallor, 20% had cyanosis, 4.2% had clubbing, and 43.3% had edema and raised JVP respectively.

Chart 7: Bar diagram showing physical signs among patients with Heart Failure

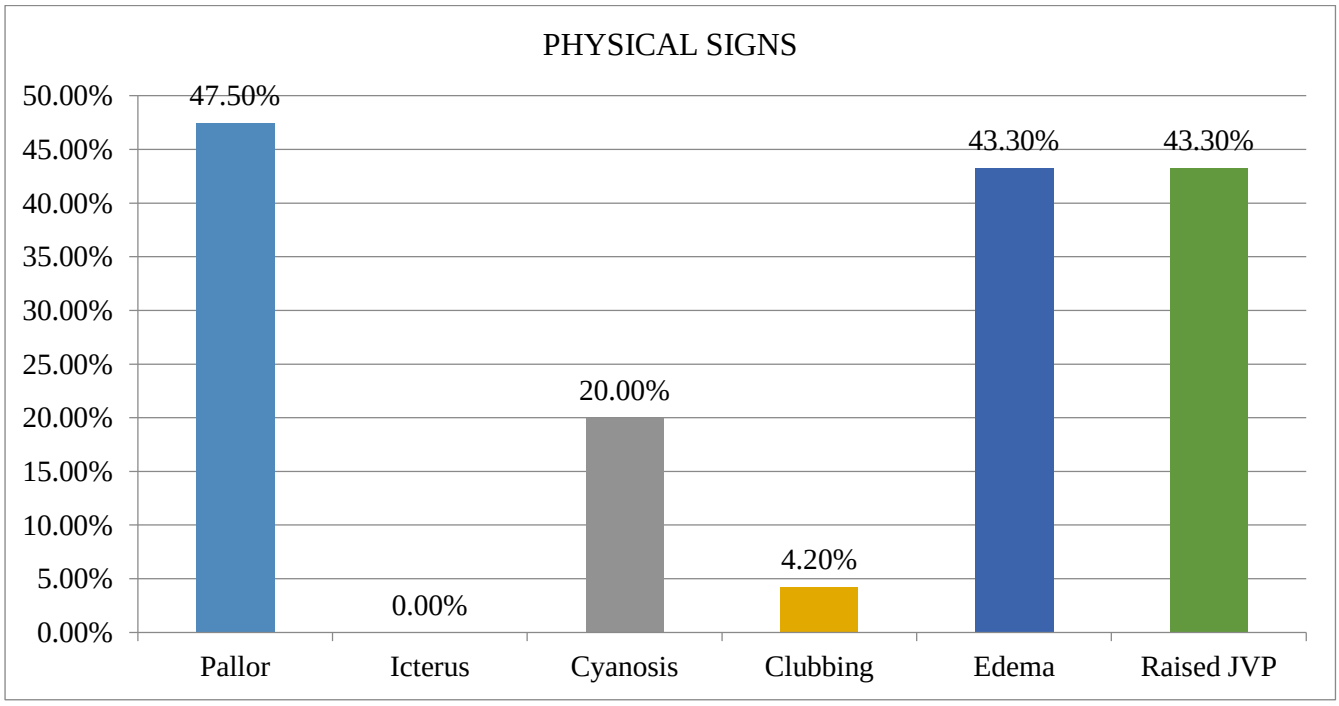


Table 17: Vital Parameters among patients with Heart Failure

		Count	%
Pulse Rate	Normal	5	4.2%
	Tachycardia	90	75.0%
	Atrial Fibrillation	25	20.8%
Blood pressure	Normal	9	7.5%
	Pre hypertension	32	26.6%
	Stage 1	32	26.7%
	Stage 2	42	32.5%
	Isolated Systolic HTN	5	4.2%
Respiratory rate	Normal	3	2.5%
	Tachypnea	117	97.5%

In the study 75% had tachycardia, 20.8% had atrial fibrillation. 26.7% had stage 1 HTN, 32.5% had stage 2 HTN and 4.2% had isolated systolic HTN

Chart 8: Bar diagram showing Vital Parameters among patients with Heart Failure

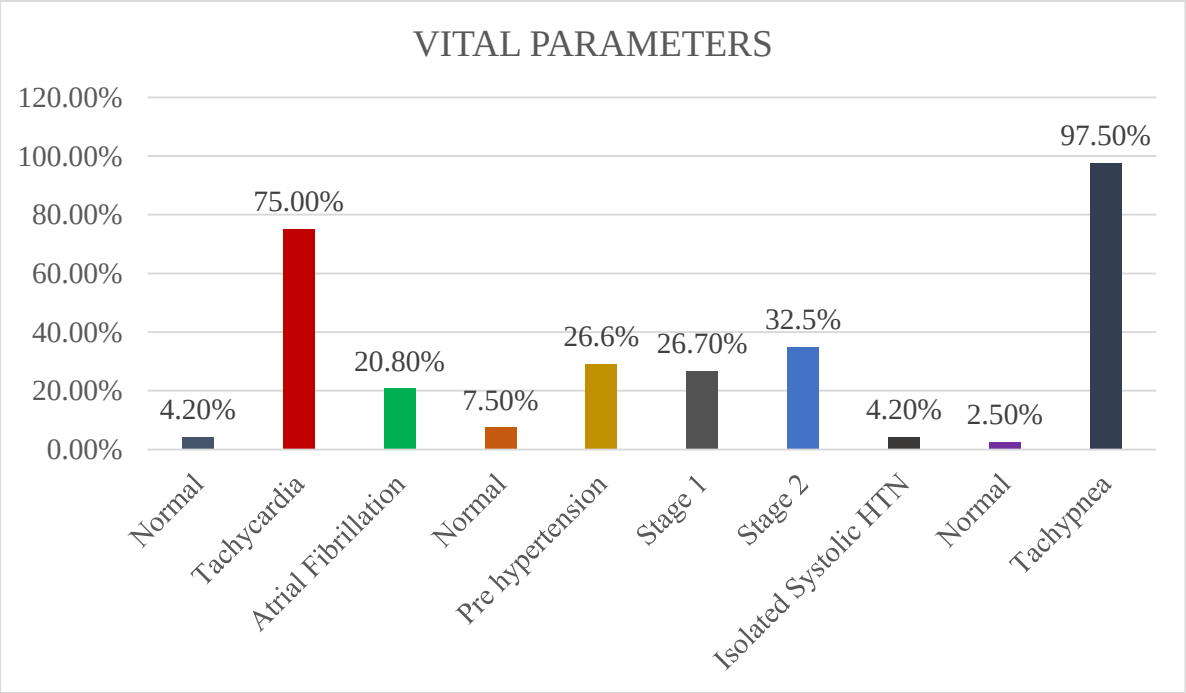


Table 18: Systemic Findings among patients

		Count (n = 120)	%
CVS*	Normal	44	36.67
	S3/S4 Present	56	46.67
	Pan systolic Murmur	17	14.17
	Ejection Systolic Murmur	17	14.17
RS*	Basal Crepitations	93	77.50
	Generalized Crepitations	19	15.83
	Rhonchi	22	18.33
	Right Pleural Effusion	2	1.67
	B/L Pleural Effusion	3	2.50
	Pneumonia	3	2.50
Per Abdomen	Normal	90	75.0%
	Right Hypochondriac tenderness	24	20.0%
	Hepatomegaly	6	5.0%
CNS	Normal	106	88.3%
	Drowsy	14	11.7%

*Multiple findings can be present for a patient

On CVS systemic examination, 46.67% had S3/S4, 14.17% had pan systolic murmur and ejection systolic murmur respectively. On RS examination 77.5% had basal Crepitations, 15.83% had generalized Crepitations, 1.67% had right pleural effusion, 2.5% had B/L pleural effusion had pneumonia respectively.

Chart 9: Bar diagram showing Systemic Findings among patients

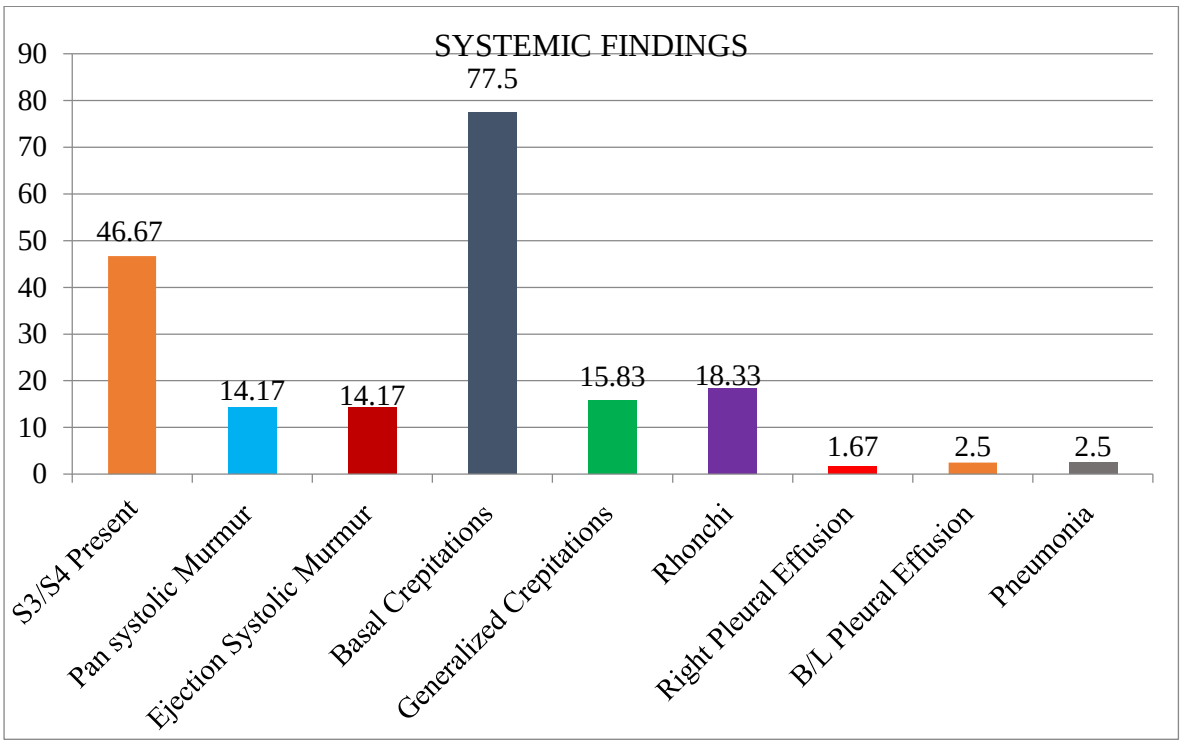


Table 19: Hb% among patients with Heart Failure

		Count	%
Hb%	Normal	63	52.5%
	Anaemia	57	47.5%
	Total	120	100.0%

In the study 47.5% were anaemic.

Chart 10: Pie diagram showing Hemoglobin % among patients with Heart Failure

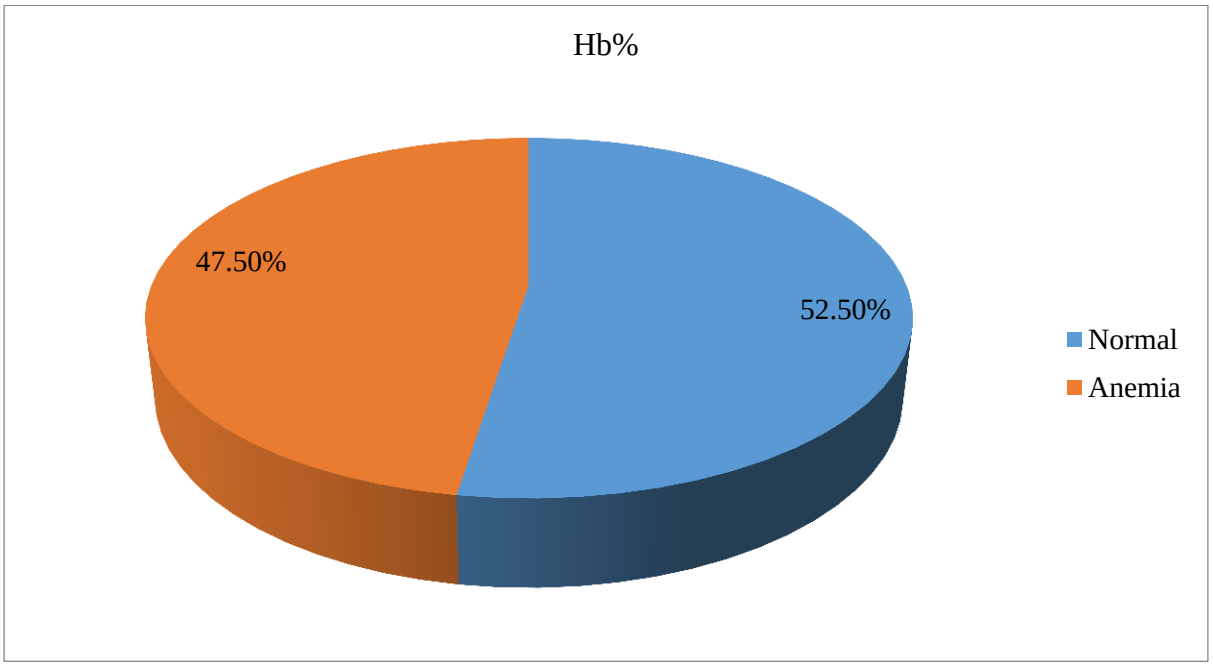


Table 20: Thyroid function among patients with Heart Failure

		Count	%
TSH	Normal	110	91.7%
	Hypothyroidism	7	5.8%
	Hyperthyroidism	3	2.5%
	Total	120	100.0%

5.8% were hypothyroid and 2.5% were hyperthyroid.

Chart 11: Pie diagram showing Thyroid function among patients with Heart Failure

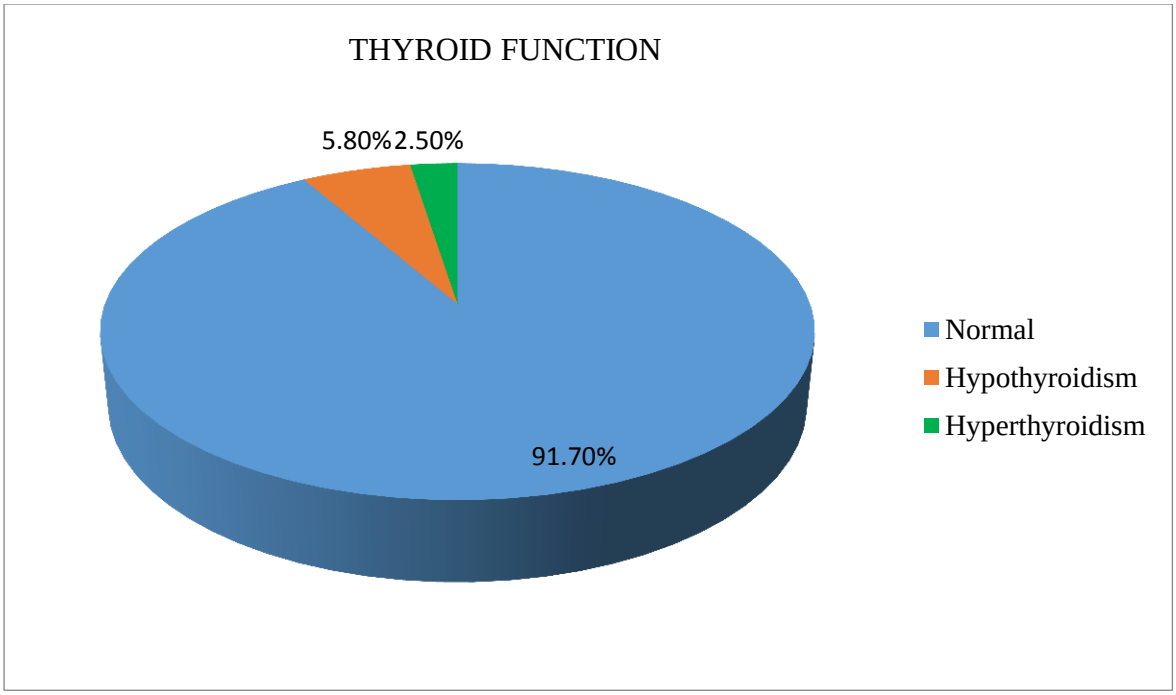


Table 21: Chest X ray findings among patients

		Count	%
Chest X Ray	Normal	32	26.67
	Cardiomegaly	49	40.83
	Pulmonary Edema	49	40.83
	Effusion	15	12.50
	COPD	14	11.67
	Pneumonia	6	5.00

*Multiple findings can be present for a patient

On chest X ray, 40.83% had Cardiomegaly and pulmonary edema, 12.5% had effusion, 11.67% had COPD and 5% had pneumonia.

Chart 12: Bar diagram showing Chest X ray findings among patients

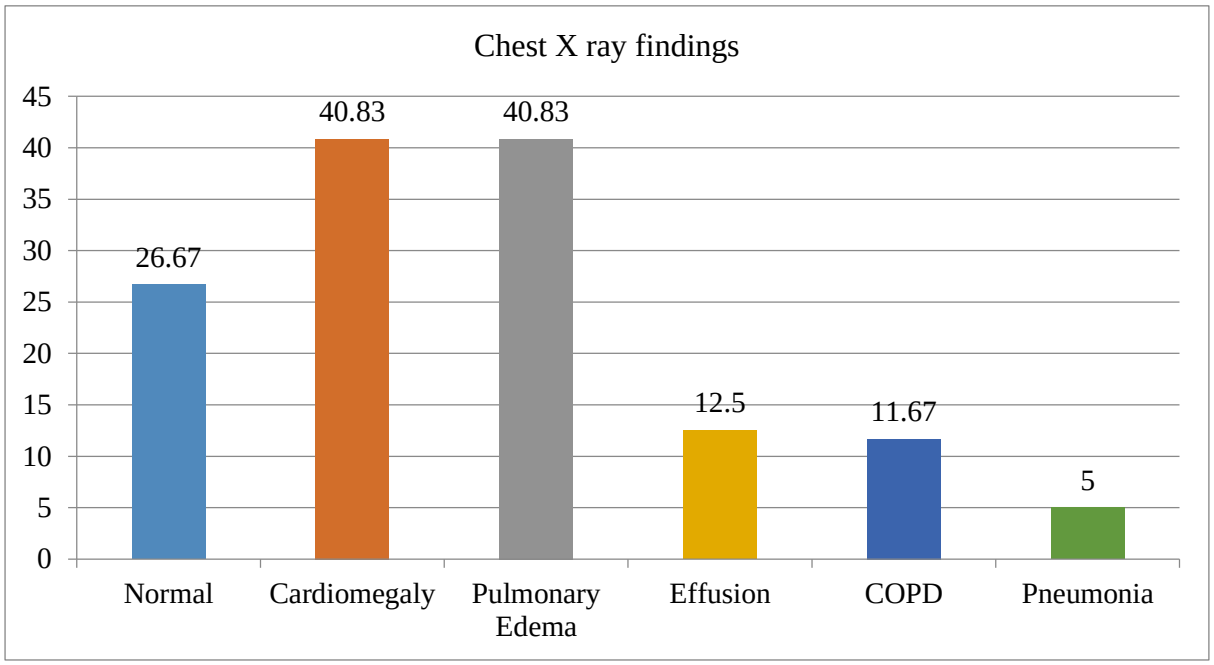


Table 22: ECG Findings among patients with Heart Failure

		Count	%
Rhythm	Normal	5	4.2
	Sinus Tachycardia	90	75.0
	Atrial fibrillation	25	20.8
Chamber Size	Left ventricular hypertrophy	87	72.5
	Biventricular hypertrophy	21	17.5
	Left atrial enlargement	45	37.50
	Right atrial enlargement	17	14.17
	Normal	19	15.80
Ischemia	Present	67	55.8%
	Absent	53	44.2%

*Multiple findings can be present for a patient

75% had sinus tachycardia, 20.8% had atrial fibrillation, 72.5% had LVH,17.5% had BVH, 37.5% had LAH, 14.17% had RAH. 55.8% had ischemia.

Chart 13: Bar diagram showing ECG findings in heart failure patients

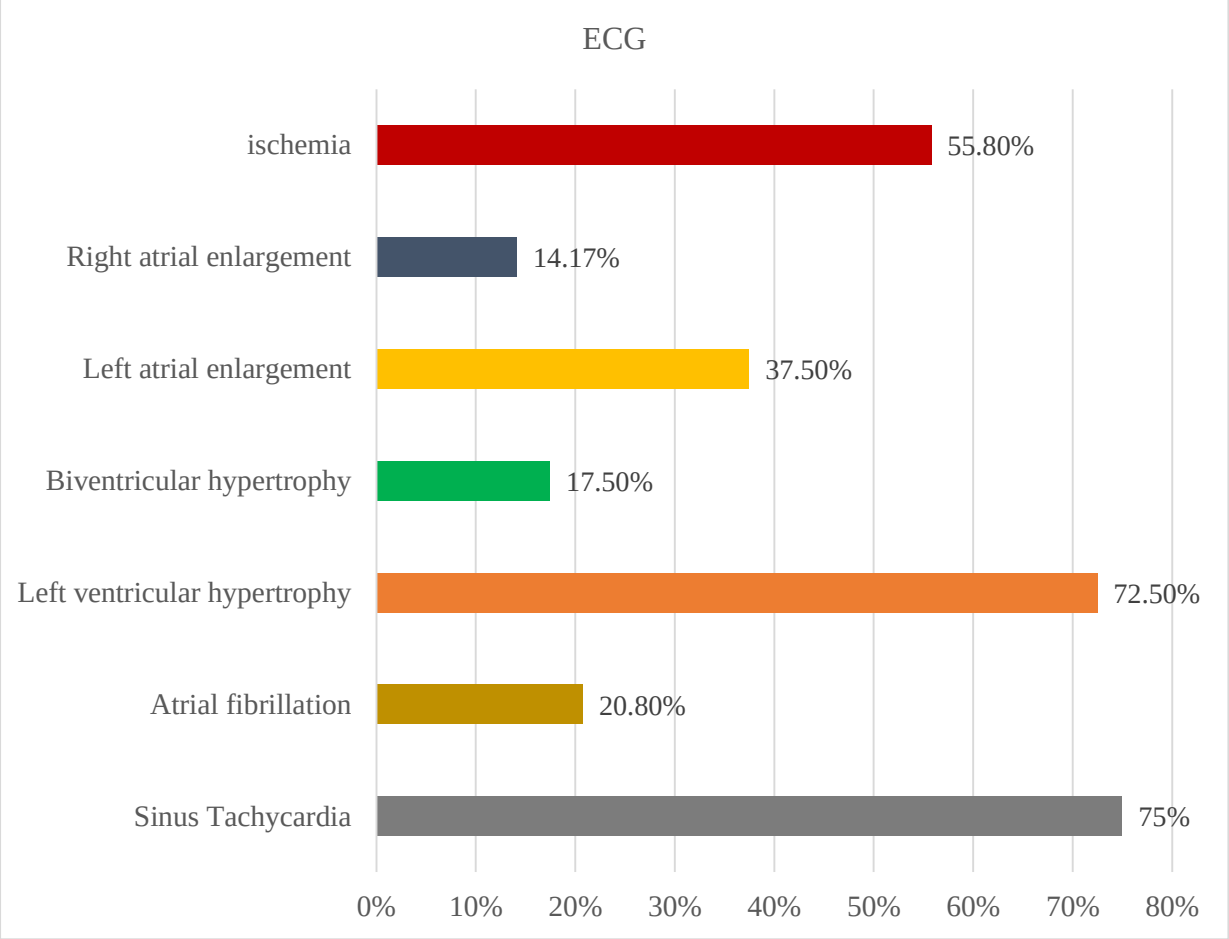


Table 23: ECHO Findings among patients with Heart Failure

Chamber enlargement*	Normal chamber size	19	15.80
	Left Ventricular Hypertrophy	89	74.2
	LA dilatation	46	38.3
	RV dilatation	27	22.50
	Bi ventricular hypertrophy with LA, RA dilatation	23	19.2
Ejection Fraction	<40%	61	50.9%
	40-49%	10	8.3%
	≥50%	49	40.8%
Pulmonary Hypertension	Mild to Moderate	21	17.5%
	Severe	17	14.2%
	Normal	82	68.3%
Valve Lesions	Present	30	25.0%
	Absent	90	75.0%

*Multiple findings can be present for a patient

74.2%% had LVH, 38.3% had LAH, 22.5% had RV dilatation,19.2% had BVH 59.2% had Ejection fraction <50% and 40.8% had Ejection fraction > 50%. 17.5% had mild to moderate Pulmonary HTN and 14.2% had Severe HTN, 25% had valve lesions.

Chart 14: Bar diagram showing ECHO Findings among patients with Heart Failure

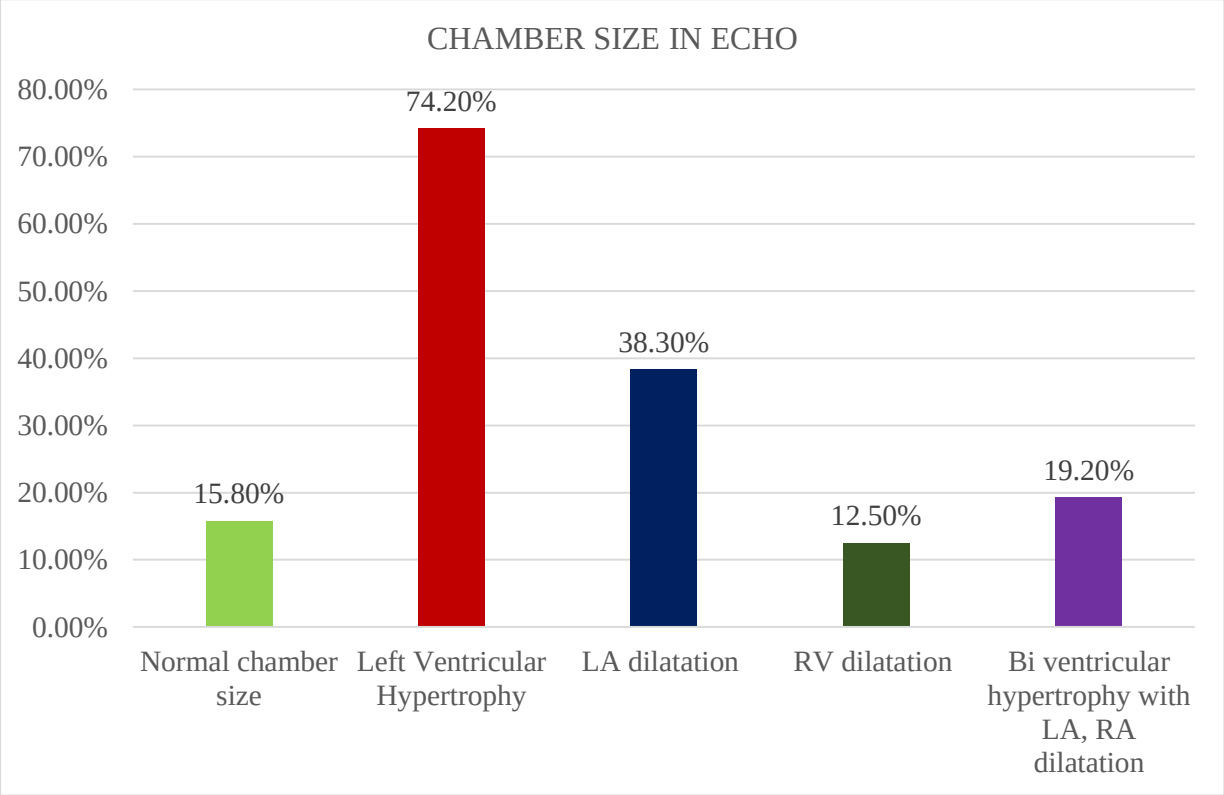


Chart 15: Pie diagram showing Ejection Fraction among heart failure

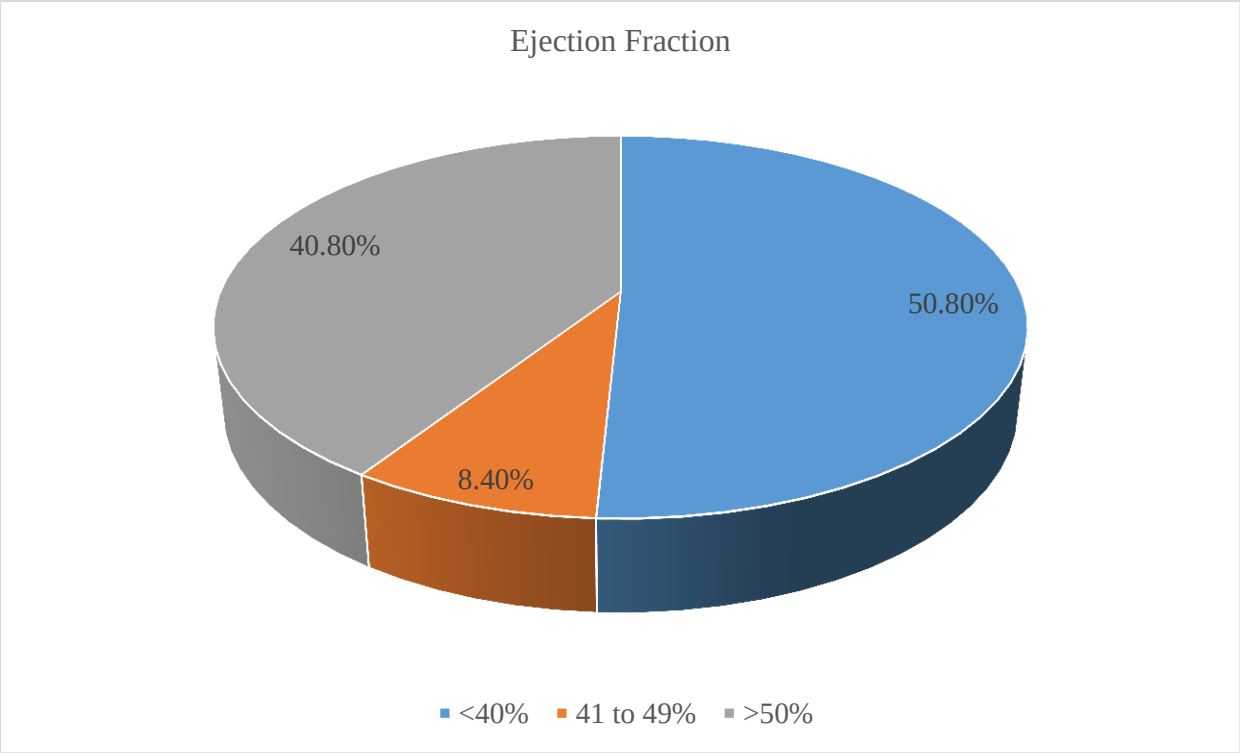


Table 24: Gender distribution among heart patients with EF <40% and EF ≥ 50%

GENDER	EF <40%	EF ≥ 50%
Males	43 (70.49%)	18 (36.73%)
females	18 (29.5%)	31(63.26%)

In study patients with EF < 40% majority were males 70.49% and patients with EF ≥50% majority were females

Chart 16: Gender distribution among heart patients with EF <40% and EF ≥ 50%

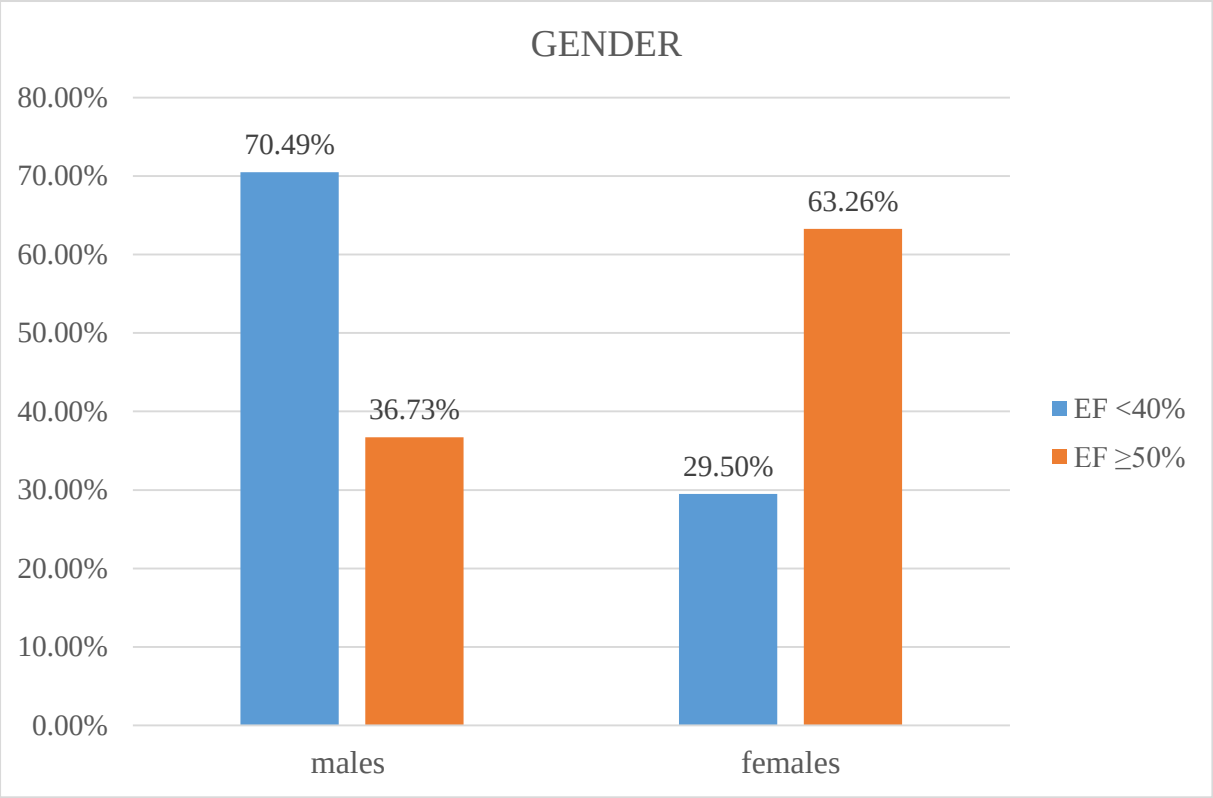


Table 25: Age distribution among heart patients with EF <40% and EF ≥ 50%

Age	EF <40%	EF ≥ 50%
<50 years	19 (27.53%)	2 (4.10%)
51-75 years	39 (63.93%)	27 (55.10%)
>75 years	3 (4.98%)	20 (40.82%)

Majority of patients were in the age group 51 to 75 years.

Chart 17: Age distribution among heart patients with EF <40% and EF ≥ 50%

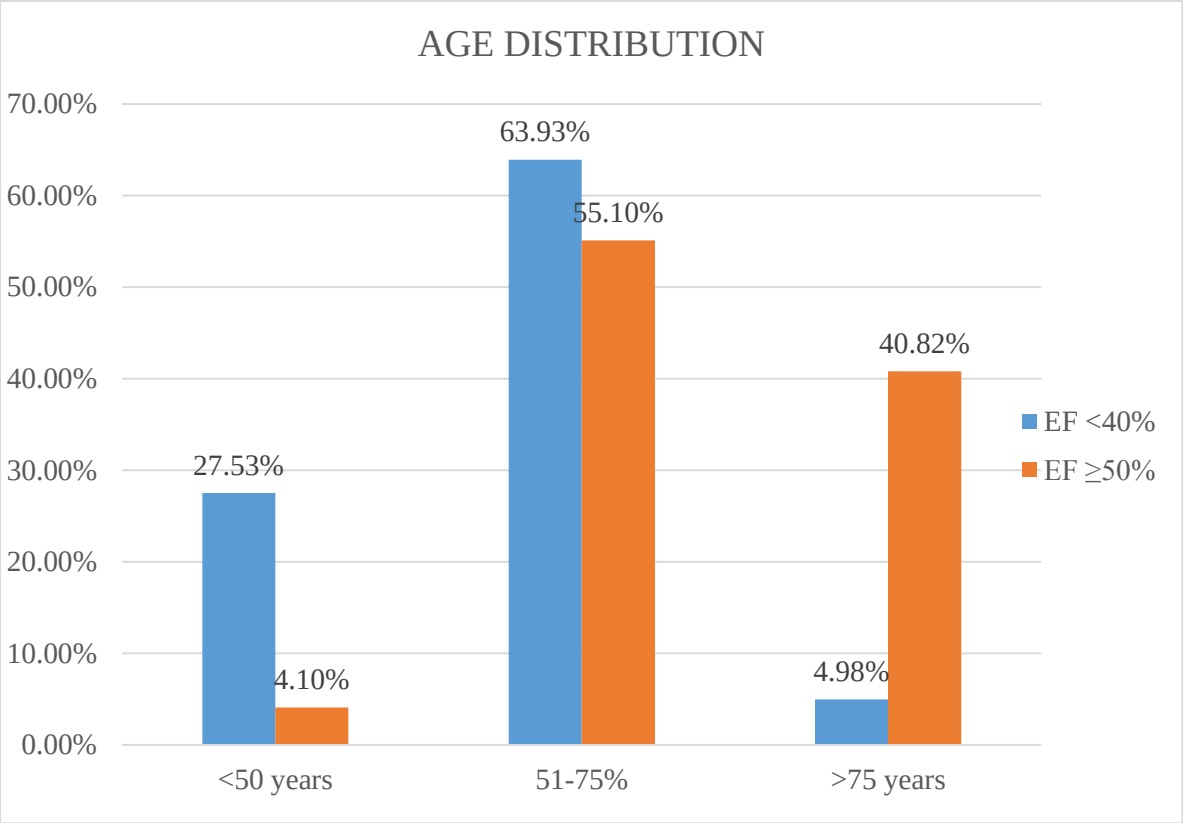


Table 26: Association between Breathlessness grade and Ejection fraction among subjects with heart failure

		Ejection Fraction			
		<40%		≥50%	
		Count	%	Count	%
Breathlessness	Grade I	5	8.1%	6	12.2%
	Grade II	17	27.9%	11	22.44%
	Grade III	23	37.8%	18	36.7%
	Grade IV	16	26.2%	11	22.44%
	No breathlessness	0	0%	3	6.1%
	Total	71	100.0%	49	100.0%

χ 2 = 10.502, df = 4, p = 0.033*

In the study significant association was observed between Ejection fraction and Breathlessness. Among subjects with EF <40% and EF ≥ 50%, majority of them presented with EF grade III respectively. Grade II and Grade IV breathlessness was common in subjects with EF ≥ 50%.

Chart 18: Bar diagram showing Association between Breathlessness grade and Ejection fraction among subjects with heart failure.

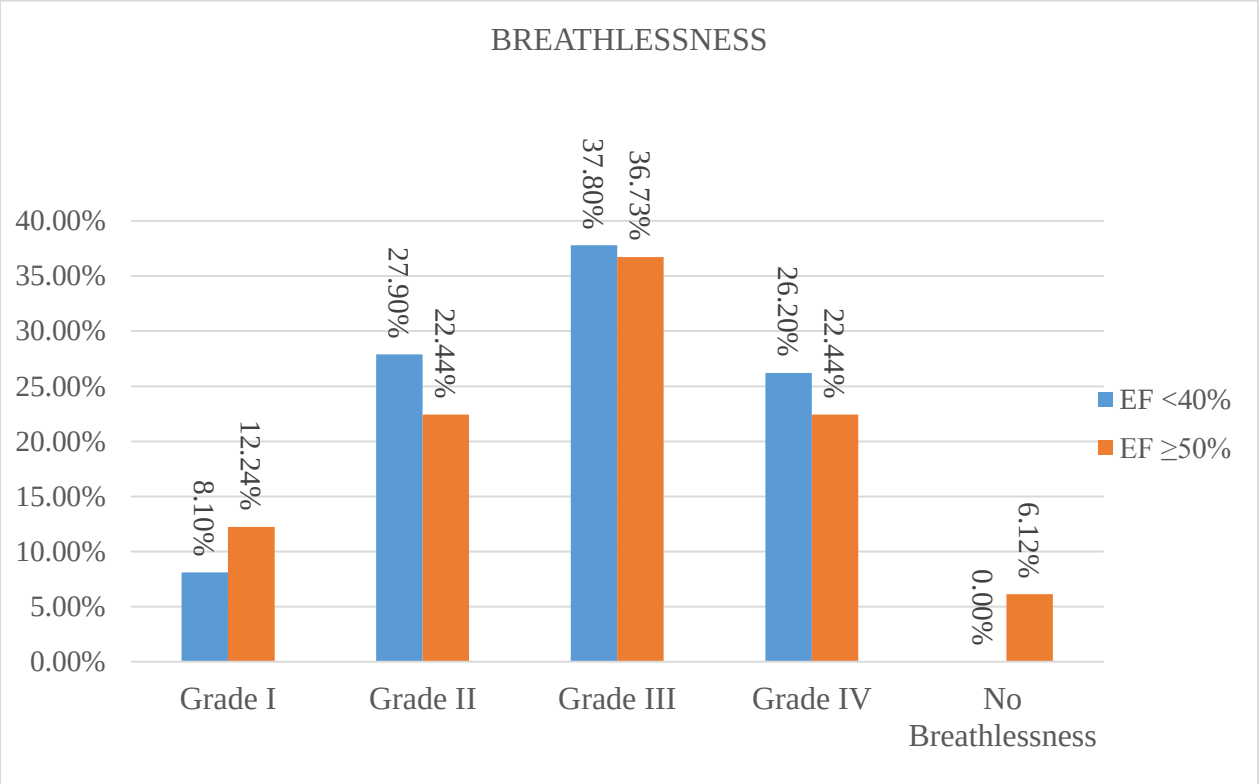


Table 27: Association between Ejection fraction and symptoms among subjects with heart failure

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Lower Limb Swelling	Present	22	36.1%	21	42.9%	0.468
	Absent	39	63.9%	28	57.1%	
Cough	Present	33	54.1%	23	46.9%	0.455
	Absent	28	45.9%	26	53.1%	
Palpitations	Present	27	44.3%	17	34.7%	0.309
	Absent	34	55.7%	32	65.3%	
Chest Pain	Present	24	39.3%	24	49.0%	0.311
	Absent	37	60.7%	25	51.0%	
Fever	Present	17	27.9%	12	24.5%	0.689
	Absent	44	72.1%	37	75.5%	

In the study no significant difference was observed between Ejection fraction and symptoms on presentation

Chart 19: Bar diagram showing Association between Ejection fraction and symptoms among subjects with heart failure

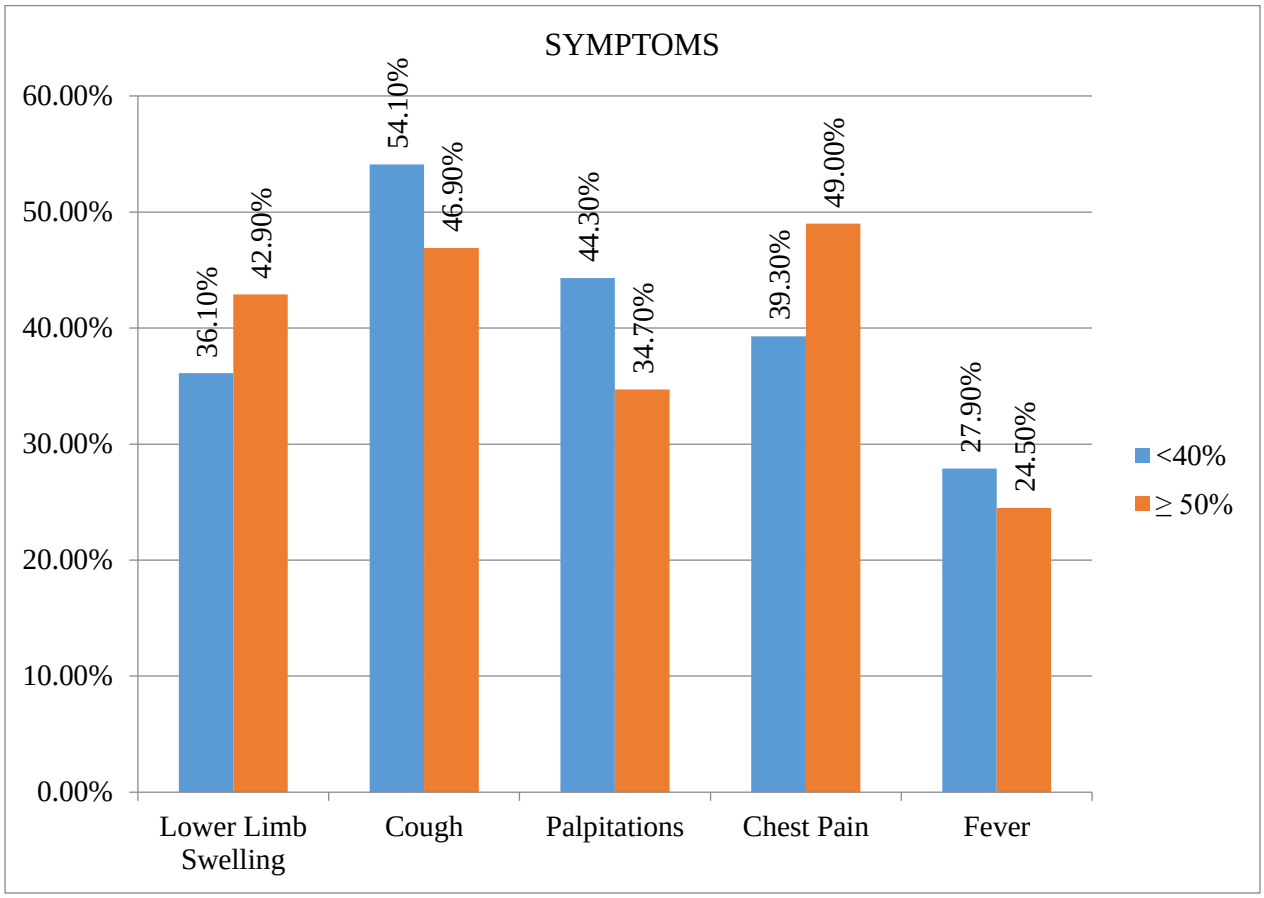


Table 28: Association between Ejection fraction and comorbidities among subjects with heart failure

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Hypertension	Present	35	57.4%	33	67.3%	0.285
	Absent	26	42.6%	16	32.7%	
Coronary Artery Disease	Present	46	75.4%	11	22.4%	<0.001*
	Absent	15	24.6%	38	77.6%	
Diabetes Mellitus	Present	39	63.9%	29	59.2%	0.610
	Absent	22	36.1%	20	40.8%	
Atrial Fibrillation	Present	10	16.4%	11	22.44%	0.785
	Absent	51	83.6%	40	81.6%	
COPD	Present	21	34.4%	17	34.7%	0.977
	Absent	40	65.6%	32	65.3%	
Valvular heart diseases	Present	4	6.6%	7	14.3%	0.179
	Absent	57	93.4%	42	85.7%	

In Subjects with EF <40%, 75.4% had CAD and with EF ≥ 50% 22.4% had CAD. This difference was statistically significant.

No significant difference in other co morbidities was associated with Ejection fraction.

Chart 20: Bar diagram showing Association between Ejection fraction and comorbidities among subjects with heart failure

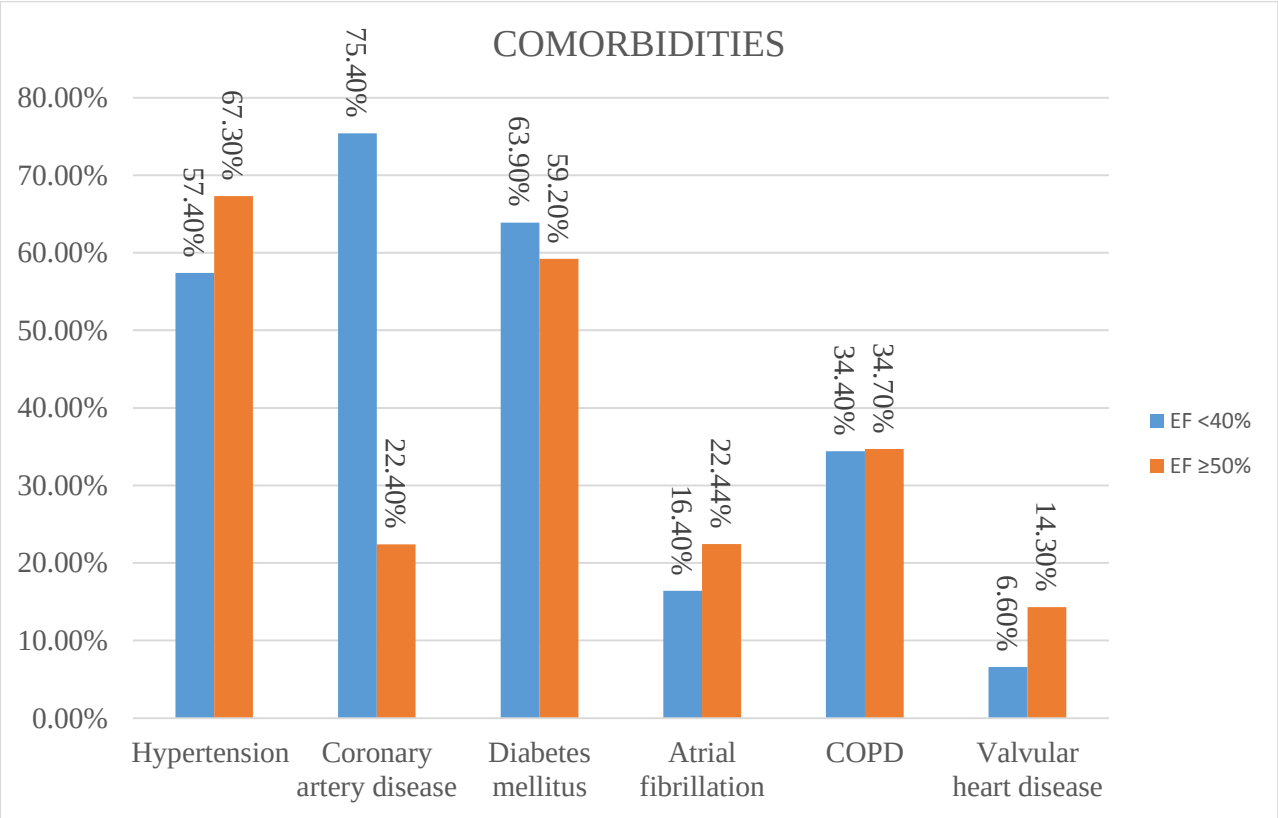


Table 29: Association between Ejection fraction and physical signs among subjects with heart failure

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Edema	Present	29	47.5%	19	38.8%	0.357
	Absent	32	52.5%	30	61.2%	
JVP	Raised	25	41.0%	22	44.9%	0.680
	Normal	36	59.0%	27	55.1%	
Pulse Rate	Normal	2	3.3%	1	2.0%	0.297
	Tachycardia	49	80.3%	34	69.4%	
	Atrial Fibrillation	10	16.4%	14	28.6%	
Blood pressure	Normal	4	6.6%	5	10.2%	0.802
	Pre hypertension	22	36.1%	13	26.5%	
	Stage 1	15	24.6%	15	30.6%	
	Stage 2	18	29.5%	14	28.6%	
	Isolated Systolic HTN	2	3.3%	2	4.1%	

No significant difference was observed between Ejection fraction and edema, JVP, Pulse rate and blood pressure.

Chart 21: Bar diagram showing Association between Ejection fraction and GPE among subjects with heart failure

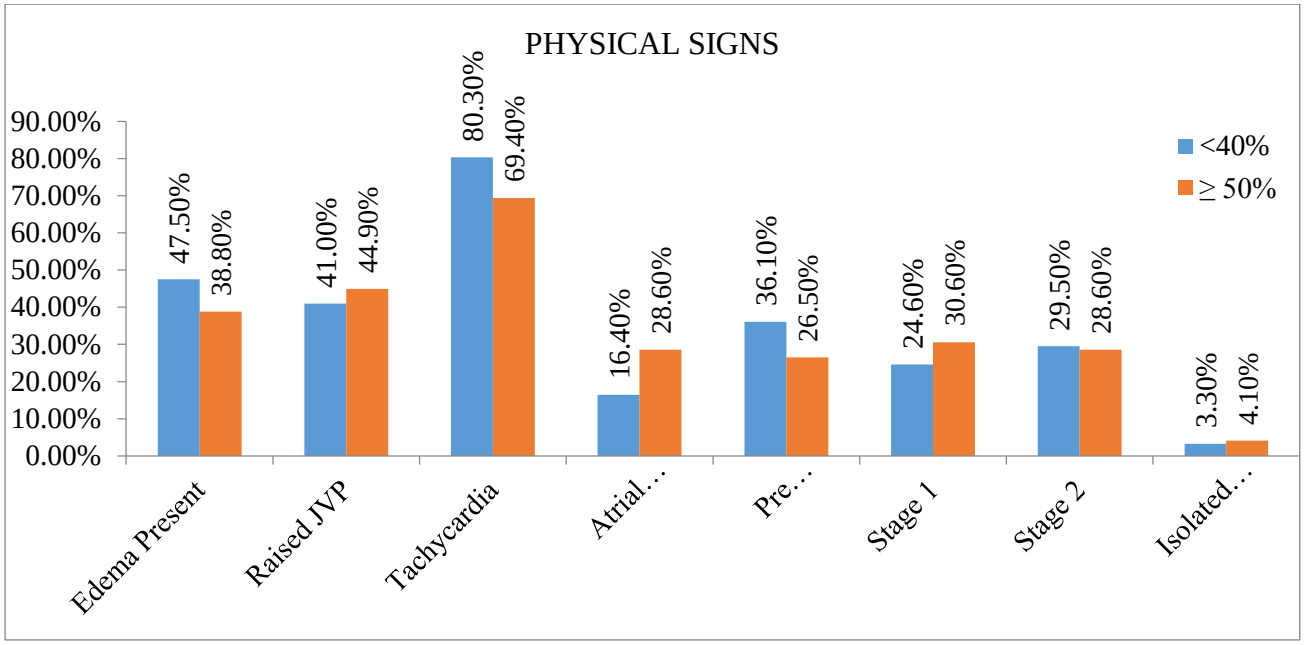


Table 30: Association between Ejection fraction and Hb% and TSH among subjects with heart failure

		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Hb%	Normal	26	42.6%	33	67.3%	0.01*
	Anemia	35	57.4%	16	32.7%	
TSH	Normal	54	88.6%	47	95.9%	0.185
	Hypothyroidism	5	8.2%	1	2.0%	
	Hyperthyroidism	2	3.2%	1	2.0%	

In subjects with EF <40%, 57.4% had anemia and with EF ≥ 50%, 32.7% had anemia. This observation was statistically significant.

No significant difference was observed between thyroid profile and EF.

Chart 22: Bar diagram showing Association between Ejection fraction and Hb% among subjects with heart failure

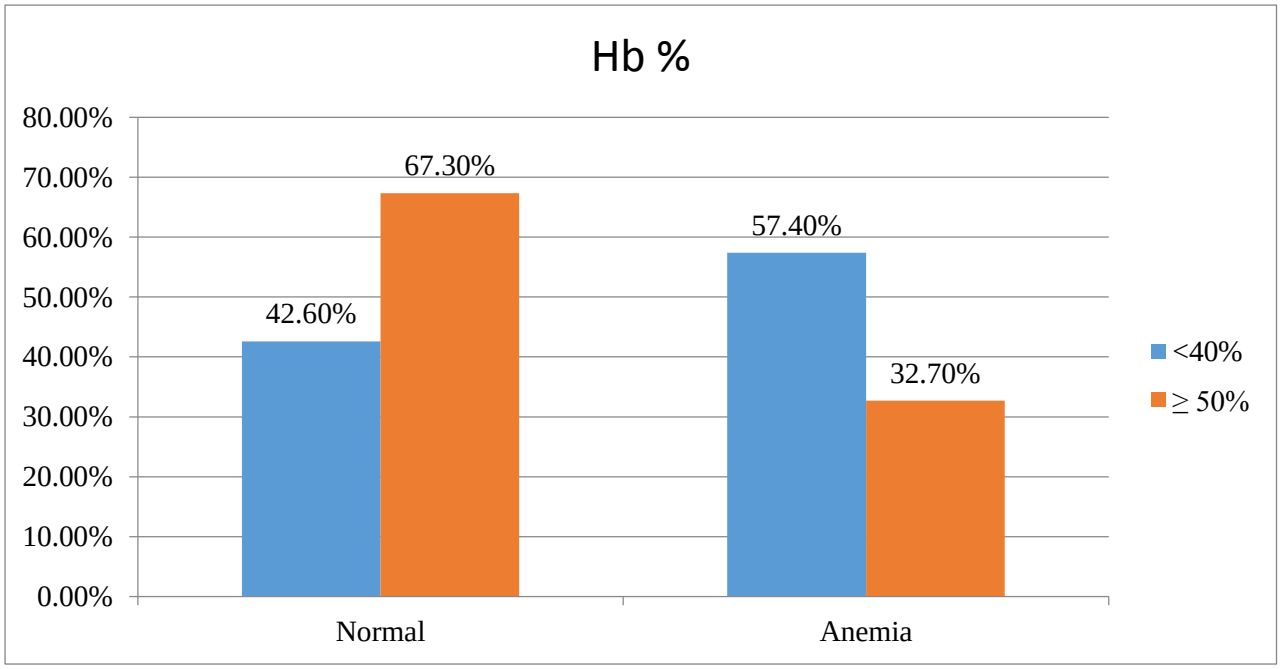


Chart 23: Bar diagram showing Association between Ejection fraction and thyroid functions among subjects with heart failure

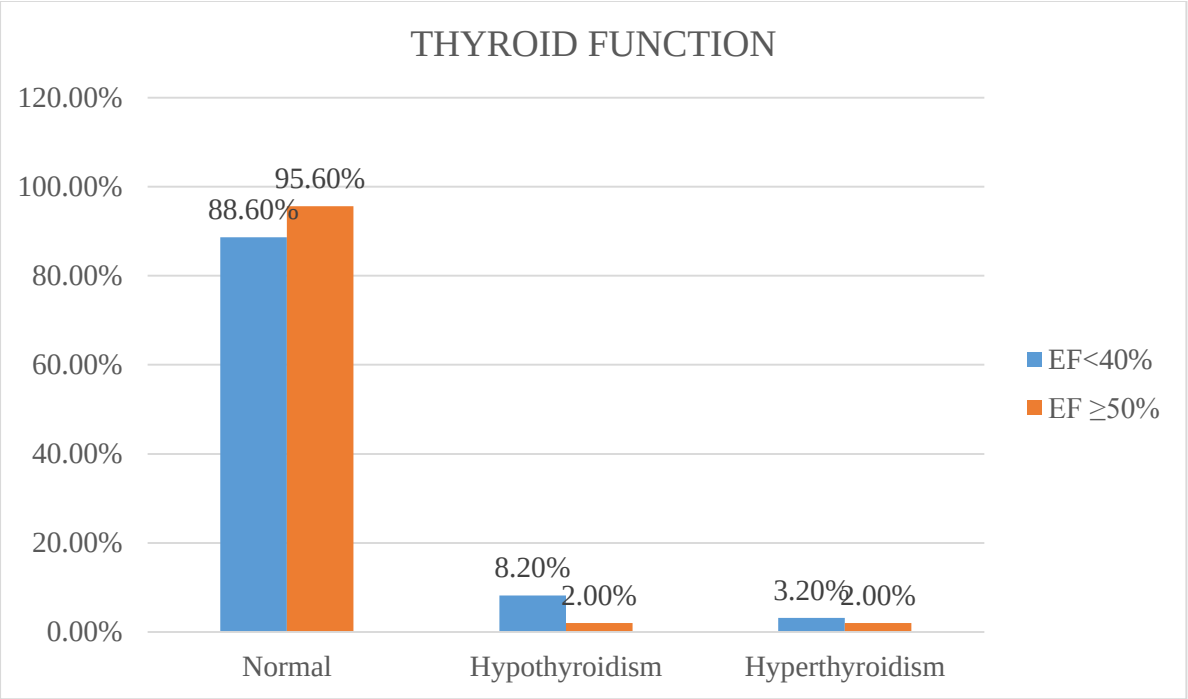


Table 31: Association between Ejection fraction and ECG changes among subjects with heart failure

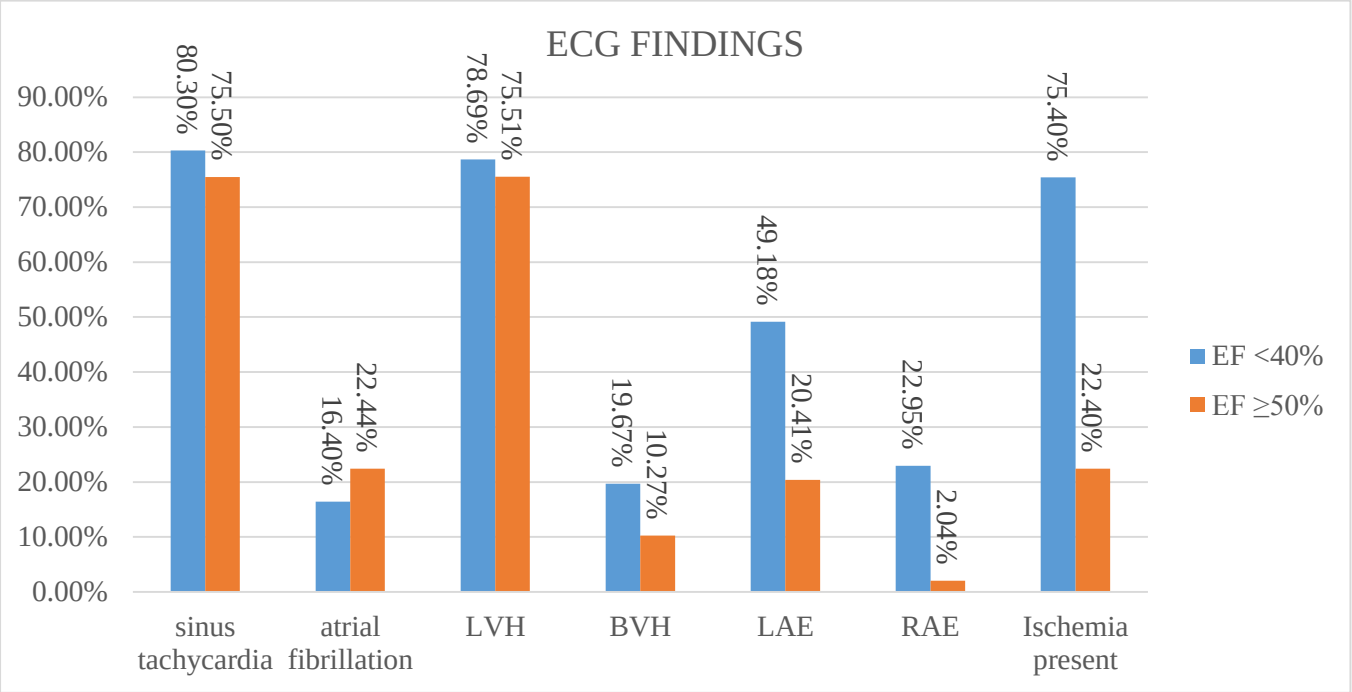
		Ejection Fraction				P value
		<40%		≥ 50%		
		Count	%	Count	%	
Rhythm	Normal	2	3.3%	1	2.0%	0.297
	Sinus Tachycardia	49	80.3%	37	75.5%	
	Atrial fibrillation	10	16.4%	11	22.44%	
Chamber Size	LVH	48	78.69%	37	75.51%	<0.001*
	BVH	12	19.67%	5	10.20%	
	LAE	30	49.18%	10	20.41%	
	RAE	14	22.95%	1	2.04%	
	Normal	5	8.20%	11	22.45%	
Ischemia	Present	46	75.4%	11	22.4%	<0.001*
	Absent	15	24.6%	38	77.6%	

In subjects with EF <40%, 80.3% had sinus tachycardia, 16.4% had atrial fibrillation. Similarly, in subjects with EF ≥ 50% 75.5%% had sinus tachycardia and 22.44% had atrial fibrillation.

In subjects with EF <40%, 78.69% had LVH, 19.67% had BVH, 49.18% had LAE and 22.95% had RAE. In subjects with EF ≥ 50%, 75.51% had LVH, 10.20% had BVH, 20.41% had LAH and 2.04% had RAH. This observation in chamber size between EF was statistically significant.

In subjects with EF <40%, 75.4% had Ischemic changes and in subjects with EF > 50%, 22.4% had ischemic changes. This observation was statistically significant.

Chart 24: Bar diagram showing Association between Ejection fraction and ECG findings among subjects with heart failure



DISCUSSION

Heart failure is a common and a major health problem and its prevalence increases with age. Epidemiological studies have revealed that 1.5% to 2% population experience heart failure (HF) and it is the main reason for hospital admission of elderly patients.[104] It has been estimated that the prevalence increases to 6% - 10% in patients over 65 years of age.[105,106] The increasing mean life expectancy, together with improved survival rates in patients with other cardiovascular diseases and after myocardial infarction, is expected to result in a major increase in the prevalence of heart failure in the future.[107]

Although the diagnosis of HF can be straightforward when the patient presents with a constellation of the classic signs and symptoms in the appropriate clinical setting, no sign or symptom alone can define the presence or severity of HF. Furthermore, the detection of diagnostic physical findings in HF is an imprecise science, often requiring other diagnostic tools. Because treatment strategies for treating HF are based on the differentiation of HFrEF and HFpEF, these distinctions are crucial.[108]

There are only a few Indian population based studies comprehensively and prospectively assessing the demographic, clinical and prognostic characteristics of patients who are admitted with a clinical diagnosis of HF. Hence this study was undertaken to know the common clinical presentation and comorbidities precipitating HF. Differentiating HFrEF and HFpEF helps in assessing the prognosis and planning the appropriate treatment modality.

In our study, a total of one hundred and twenty patients satisfying Framingham's criteria for heart failure were included.

A study done by Laxman Dubey et al [109] and Okechukwu S et al [110] showed that the incidence of heart failure increases with age and is more common in age groups between 45 to 65 years which was similar to our study.

First common presenting symptom was breathlessness in studies done by Karl Swedberg , Joh Cleland et al[111] and Roby A et al [112] which was similar to our study.

Second common symptom was cough with or without expectoration (50.8%) followed by chest pain (41.7%), palpitations (38.3%), lower limb swelling (37.5%) and fever (26.7%)in our study compared to study done by Roby et al[112] where palpitation (32.54%) was second common symptom followed by chest pain (30.76%), leg swelling (26.6%) and fatigue (22.48%).

In present study, it was found that pallor was the first common sign among heart failure patients followed by ankle oedema and raised JVP compared to study done by Roby et al[112] which showed that elevated JVP (85%) was commonest sign followed by peripheral oedema (32. 5%).

In the present study, 75% of patients had sinus tachycardia,20.8% patients had atrial fibrillation, 29.2% had pre hypertension, 26.7% had stage 1 HTN, 35.0% had stage 2 HTN and 4.2% had isolated systolic HTN,97.5% patients had tachypnea at the time of presentation,45.67% had s3/s4 on CVS examination,77.50% had basal crepitations and 18.33% had rhonchi.

In a study done by Roby et al[112] and Laxman Dubey[109], basal crackles were present in 89.94% and 68% respectively compared to our study in which 77.5% patients had basal crepitations.

In our study, smoking was observed in 34.2% and alcohol consumption in 30% patients compared to other studies done by Urban Alehagen[113] where smoking was observed in 38% patients, alcohol consumption in 45% patients and study by Jacob V. Jose observed[114] smoking in 27% patients and alcohol consumption in 37% patients and in study by Francesca Bursi et al[115] showed smoking in 58% as risk factors for heart failure.

Comorbid Conditions not only represent diseases that are risk factors for the development of heart failure but also can complicate diagnosis and management. In our study 65.8% had HTN which is the most common comorbidity followed by diabetes mellitus in 61.7% and CAD in 55.8% compared to study by Okechukwu S et al[110] where hypertension was the most common comorbidity present in 78.5% of cases. This finding is consistent with our study. Studies done by Adams KF et al [116] and Nieminen MS et al[117] also showed similar observations. Our study is differing from study done by Laxman Dubey et al[109] where CAD (36.5%), was the most common comorbidity leading to HF followed by valvular heart disease (25.5%) and hypertensive heart failure (8.6%).

In our study valvular heart disease was present in 10% of HF patients which was differing from the study by Laxman Dubey et al [109] where valvular heart diseases was present in 22.5% of HF patients.

In a study done by Di Marcco JP et al[118]atrial fibrillation was present in 42% compared to present study where atrial fibrillation was present in 20.8% of heart failure patients.

In our study COPD was present in 34.2% of HF patients and this observation is similar to study by Mentz RJ [119] which showed COPD in 35% of HF patients.

A systemic review and meta-analysis study by Hessel.F.Groenveld et al[120] showed anemia in 37.2% of HF patients whereas our study showed anemia in 47.5% of HF patients. Anemia may lead to increased work load, resulting from an increased heart rate and stroke volume. In response to increased workload, heart undergoes remodelling, marked by LV hypertrophy and dilatation leading to HF.[121]

In our study 91.7% of HF patients had normal thyroid function , 5.8% patients had hypothyroidism and 2.5% of patients had hyperthyroidism compared to study done by Judith E. Mitchell[122] which showed similar observations i.e majority (87%) had normal TSH levels

(0.3 to 5.0 μU/ml) at baseline, 12% had hypothyroidism and 1% had hyperthyroidism. Majority of HF patients are euthyroid in this study which is consistent with our study.[122]

Majority of HF patients in our study had cardiomegaly and pulmonary edema (40.83%) followed by effusion in 12.5%.

ECG showed sinus tachycardia and AF in 75.0% and 20.8% patients respectively. LVH was found in72.5% patients followed by biventricular hypertrophy in 17.5% patients, LA (Left atrium) hypertrophy/dilatation in 37.5% patients, RA (Right atrium) hypertrophy/dilatation in 14.2% patients in our study.

In our study 2D Echocardiography of HF patients showed EF of <40% in 50.9% of patients (HFrEF), EF of 40-49% in 8.3% of patients (HFmrEF) and EF ≥50% in 40.8% of patients(HFpEF) compared to studies done by Stella M et al[123] and Yancy CW et al[124] where systolic dysfunction was detected in 58.5% and preserved systolic function in 41.5%.[123] This finding in our study is differing from the largest population based study in India done by Chaturvedi et al [125] which showed that 67% of HF patients had preserved left ventricular (LV) systolic function and 33% had LV systolic dysfunction.

PRESERVED (> 50%) VERSUS REDUCED (<40%)EJECTION FRACTION

In our study out of 120 patients, 61(50.8%) had HFrEF, 49 (40.8%) had HFpEF. Most common age group among patients with preserved and reduced EF is between 51 to 75 years (55.10% versus 63.93%respectively).

Most of the patients of age >75 years were females (20 patients out of 25) and had HFpEF in our study that is similar to data from ADHERE registry[126] which showed that women admitted for HF were older than men (74 versus 70 years), and more frequently had preserved systolic function (51% versus 28%).

No significant difference was observed in symptoms and signs on presentation in both patients of HFpEF and HFrEF.

Among patients with EF <40% and EF ≥50%, majority of them presented with breathlessness of grade III respectively. In this study significant association was observed between ejection fraction and breathlessness. This observation is similar to other study done by Stella M et al.[123]

Our study showed that 57.7% of HFrEF patients had anemia and 32.7% of HFpEF had anemia. This observation was statistically significant in our study and this observation was differing from study done by Inder S Anand et al[121] which showed no significant difference in the distribution of anemia in both the groups of HF patients.

No significant difference was observed between thyroid profile and EF in both groups of HF patients.

In present study among HFrEF patients ,75.4% of had CAD followed by diabetes mellitus (63.9%) and hypertension (57.4%) as co-morbidities and it was similar to study done by Bocchi EA et al.[127] Coronary artery disese is more common in HFrEF patients than HFpEF group.This observation was similar with Indian population based study by Chaturvedi et al.[125]

Among HFpEF patients, hypertension was most common co-morbid condition in our study and was present in 63.7% patients. Other co-morbidities were diabetes mellitus (59.2%) and coronary artery disease (22.4%) This finding of our study was similar to study done by Fonarrow G.C et al.[128] and Chaturvedi et al[125]

In present study atrial fibrillation is more common in patients with HFpEF (22.4%) than HFrEF (16.4%). This observation was similar to study done by Rajalakshmi S et al.[129]

ECG showed ischemia in 75.4% of HFrEF patients and 22.4% of HFpEF patients in the present study and was statistically significant. Myocardial ischemia is more common in

patients with HFrEF in our study. This observation was similar to study by Chaturvedi et al.[125]

CONCLUSION

- A total of one hundred and twenty patients satisfying Framingham's criteria for heart failure were studied.
- Heart failure is more predominant in males and elderly females.
- HFpEF was more predominant in females of elderly age group
- Most common age group affected was 51- 75 years.
- Breathlessness was the commonest presenting symptom followed by cough and chest pain. Most of the patients presented with grade III breathlessness.
- Pallor followed by oedema and raised JVP are the common presenting clinical signs.
- Hypertension is the most common co-morbidity present in the HF patients in our study and majority of hypertensives were in stage II of JNC VII classification of hypertension.
- Other comorbidities are diabetes mellitus, coronary artery disease, COPD and valvular heart diseases.
- Anemia is present in significant number of HF patients in our study which carries poor prognosis.
- Majority of patients were in euthyroid state.
- Patients with HFrEF were more common than that of HFpEF. But there is increasing prevalence of HFpEF compared to past most probably because of advanced diagnostic modalities and increased life expectancy.
- No significant difference was observed in symptoms and signs on presentation in patients of both HFpEFand HFrEF.
- Anemia was more common in HFrEF patients than in HFpEF.

- Most common co-morbidity in patients of HFrEF and HFpEF is coronary artery disease and hypertension respectively.
- AF is more common in HFpEF patients than HFrEF patients and it carries poor prognosis in both groups of patients.
- Hence this study of clinical profiles reaffirms the value of clinical assessment in the daily practice of which increasingly includes heart failure.
- Clinical profiles are easy to define, predict prognosis, and appear to do so better than traditional markers of disease severity. These profiles may be useful to guide appropriate therapy.
- As the treatment modality and prognosis differs between patients of reduced and preserved EF it is important to distinguish between HFrEF and HFpEF. Non-invasive modalities like echocardiography can be effectively used to identify systolic and diastolic dysfunction in heart failure patients.
- A variety of co morbidities interplay in the pathogenesis and precipitation of heart failure, hence thorough knowledge regarding risk factors and co-morbidities is essential for appropriate and timely management.

SUMMARY

- This study was a prospective observational study done at a tertiary medical college hospital. Total of one hundred and twenty patients satisfying Framingham criteria for heart failure were studied.
- Majority of patients were in the age group of 51-75 years (61.2%) followed by >75 years (20.9%) and <50 years (17.9%).
- Males (57.5%) are most common affected than females (42.5%) in our study.
- Breathlessness is the most common presenting symptom. 117 patients out of 120 (97.5%) had breathlessness. Majority of patients presented with grade III 34.2% breathlessness followed by grade IV (26.7%), grade II (22.5%) and grade I (14.2%).
- Other presenting symptoms were cough with expectoration (50.8%), chest pain (41.7%), palpitations (38.3%), lower limb swelling (37.5%), fever (26.7%).
- 52.5% of patients had pallor followed by other physical signs like edema (43.3%)and raised JVP (43.3%).
- 34.2% were smokers and 30% were alcoholics.
- Majority of patients had hypertension (65.8%) as co-morbidity and majority of them had stage 2 HTN 32.5% followed by stage 1 HTN in 26.6% of patients.Other co-morbid conditions are diabetes mellitus(61.7%), CAD (55.8%), COPD (34.2%), AF (20.8%) and valvular heart diseases(10%).
- On systemic examination, basal crepitations were present in 77.5% of patients and s3/s4 in 46.67%.
- 47.5% of heart failure patients were anaemic and 91.7% were euthyroid.
- Chest X ray features showed cardiomegaly and pulmonary oedema in 40.83% of patients followed by 12.5% had effusion, 11.67% had COPD and 5% had pneumonia.
- 72.5% of patients had LVH and 55.8% had ischemia on ECG.

- Echocardiography showed HFrEF in50.9% and HFpEF in 40.8% of patients.
- HFpEF was most commonly observed in elderly females (63.26%)
- In the study no significant difference in symptoms and signs on presentation was observed between both groups of HFrEF and HFpEF patients.
- Statistically significant difference was seen in the distribution of CAD in patients with EF <40% and ≥ 50%.
- Most common co-morbidity in patients with HFrEF was coronary artery disease (75.4%) and in patients with HFpEF was hypertension (67.3%).
- In patients with HFrEF 75.4% had CAD and with HFpEF 22.4% had CAD. This difference was statistically significant. No significant difference in other co morbidities between both the groups of HF patients.

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ANNEXURES

INFORMED CONSENT FORM

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of my personal information as outlined in this consent form.

I understand the purpose of this study, the risks and benefits of the two techniques and the confidential nature of the information that will be collected and disclosed during the study. The information collected will be used only for research.

I have had the opportunity to ask questions regarding the various aspects of this study and my questions have been answered to my satisfaction.

I understand that I remain free to withdraw from this study at any time and this will not change my future care.

Participation in this study does not involve any extra cost to me.

Subject's name and signature /thumb impression Date:

Name and signature of witness Date:

Name and signature of person obtaining consent Date:

PROFORMA

STUDY OF CLINICAL PROFILE AND DIFFERENTIATING SYSTOLIC AND DIASTOLIC HEART FAILURE BY ECHOCARDIOGRAPHY

NAME: I.P NO.:

AGE:

SEX: BMI:

CHIEF COMPLAINTS:

BREATHLESSNESS (NYHA):

SWELLING OF LOWER LIMBS/ ABDOMINAL DISTENSION:

PALPITATION:

COUGH:

OTHER SYMPTOMS: CHEST PAIN:

ANASARCA: FEVER:

ANY OTHER/PRECIPITATING FACTORS:

PAST HISTORY:

HTN

CAD

DM

COPD

AF

FAMILY HISTORY

PERSONAL HISTORY

DIET

SLEEP

APPETITE

BOWEL AND BLADDER HABITS

ADDICTIONS:

GENERAL PHYSICAL EXAMINATION:

PALLOR/ICTERUS/CYNOSIS/CLUBBING/OEDEMA/ JVP

VITAL SIGNS: PULSE: B.P: TEMPERATURE: RESP. RATE: SPO2:

SYSTEMIC EXAMINATION:

CVS:

RESPIRATORY:

ABDOMEN:

NERVOUS SYSTEM:

LAB REPORTS

SL NO.

1. HB

2. TC

3. DC-N/L/E/M/B

4. ESR

5. PLATELETS

6. RENAL FUNCTION TESTS

- BLOOD UREA
- S. CREATININE

7. LIVER FUNCTION TEST

- BILI (T)
- BILI (D)
- S.PROTEIN
- S.ALB
- S.GLOB.
- A/G RATIO
- SGOT
- SGPT ALK. PO4 GGT

8. ELECTROLYTES

- Na+
- K+
- CL-

9. Lipid profile

10. ECG

11. CHEST X-RAY

12. 2D ECHO

13. Thyroid profile

KEY TO MASTER CHART

NAME:

AGE: <50: 1

50-75:2

>75:3

Sex: Male -1 Female -2

Breathlessness: Grade 1=1, 2=2, 3=3 4=4 no breathlessness=5

Lower limb swelling: yes=1 no =2

Cough: yes=1 no=2

Palpitation: yes=1 no =2

Chest pain: yes=1 no =2

Fever: yes=1 no =2

Hypertension: yes=1 no =2

Coronary artery disease: yes=1 no =2

Diabetes: yes=1 no =2

COPD: yes=1 no =2

Atrial Fibrillation: yes=1 no =2 old AF: 3

Valvular Heart Disease: yes=1 no =2

Pallor: yes=1 no =2

Icterus: yes=1 no =2

Cyanosis: yes=1 no =2

Clubbing: yes=1 no =2

Edema: yes=1 no =2

JVP: yes=1 no =2

Pulse: Normal: 1 Tachycardia: 2 AF :3

Blood pressure: Normal-1, Prehypertension -2, Stage1 -3, Stage2 -4, Isolated systolic hypertension -5

Respiratory rate: normal-1 tachypnea-2

CVS: Normal -1 S3/S4: 2 PSM of tricuspid regurgitation: 3 ESM of anemia: 4

RS: Basal crepts-1, Crepts all over the lung field: 2, Rhonchi: 3, Right effusion: 4, Left effusion: 5, Bilateral effusion: 6 , Pneumonia features: 7

Per Abdomen: 1- normal, 2- Right hypochondriac tenderness, 3. Hepatomegaly

CETRAL NERVOUS SYSTEM: Normal-1 drowsy- 2 other deficits – 3

Hemoglobin: normal-1 anemia-2

TSH: NORMAL: 1 Hypo:2 hyper:3

ECG: Rhythm: normal- 1 Sinus tachycardia: 2 Atrial fibrillations: 3

Chamber size: LVH-1 BVH-2 LAE-3 RAE-4 Normal-5

Ischemia: yes-1 no-2

Chest x ray: normal-1 pulmonary edema-2 effusion-3 pneumonia-4 COPD-5

6-Cardiomegaly

2D ECHO: LVH-1, Normal -2, LAE-3, RV dilatation-4,

Biventricular hypertrophy with LA, RA dilatation-5

Ejection fraction: <40%- 1, 41-49%-2, ≥50 %- 3

Pulmonary hypertension: Mild to moderate- 1 severe- 2 NO-3

Valvular Lesion: Yes-1 no – 2

INTRODUCTION

OBJECTIVES

REVIEW

OF

LITERATURE

MATERIALS

AND

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