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CONGESTIVE CARDIAC FAILURE – A DETAIL REVIEW

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ABSTRACT

Congestive cardiac failure (CCF) is a common clinical disorder that results in pulmonary vascular congestion and reduced cardiac output. CCF should be considered in the differential diagnosis of any adult patient who presents with dyspnea and/or respiratory failure. The diagnosis of heart failure is often determined by a careful history and physical examination and characteristic chest radiograph findings. The measurement of serum brain natriuretic peptide and echocardiography have substantially improved the accuracy of diagnosis. Therapy for CCF is directed at restoring normal cardiopulmonary physiology and reducing the hyperadrenergic state. The cornerstone of treatment is a combination of an angiotensin-converting-enzyme inhibitor and slow titration of a β-blocker. Patients with CCF are prone to pulmonary complications, including obstructive sleep apnea, pulmonary edema, and pleural effusions. Continuous positive airway pressure and noninvasive positive-pressure ventilation benefit patients in CCF exacerbations.

KEYWORDS: CCF, coronary artery disease, hypertension, hemodynamic changes, neurohormonal changes, cardiac glycosides.

INTRODUCTION

Congestive cardiac failure (CCF) is a chronic progressive condition that effects the pumping power of the heart muscles. While often referred to as “heart failure”, CCF specifically refers to the stage in which fluid builds up around the heart and causes it to pump inefficiently.[1] CCF is a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of CCF namely edema and rales.[2]

The incidence and prevalence of CCF is increasing. Several large clinical trials have found that pharmacological therapy results in decrease in mortality and morbidity. Despite the advances in drug therapy the morbidity and mortality of heart failure continues to remain high. Education of healthcare professionals on evidence based therapy plays an important role in successful heart failure programme. In India CHF affects younger age group but in western countries it's predominantly a disease of elderly. The important risk factors include hypertension, coronary artery disease, diabetes mellitus, valvular heart disease, cardiotoxic drugs, and obesity. In India coronary artery disease, hypertension, valvular heart diseases, diabetes mellitus and muscle diseases are the common causes for heart failure. Another common cause of heart failure in India is rheumatic heart disease.[3]

Human heart has four chambers. The upper half of the heart has two atria and the lower half has two ventricles. The ventricles pump blood to our body’s organs and tissues and the atria receive blood from our body as it circulates back from the rest of the body. CCF develops when the ventricles can’t pump blood in sufficient volume to the body.[1] As a result more blood remains in the ventricles at the end of each cardiac cycle and gradually the preload increases.[4] Eventually, blood and other fluids can back up inside the lungs, abdomen, liver and lower body.[1]

Types of CCF

Left-Sided CCF

Left-sided CCF is the most common type of CCF. It occurs when the left ventricle doesn’t properly pump blood out to the body. As the condition progresses, fluid can build up in the lungs, which makes breathing difficult.

There are two kinds of left-sided heart failure:

i. **Systolic heart failure** occurs when the left ventricle fails to contract normally. This reduces the level of

force available to push blood into circulation. Without this force, the heart can't pump properly.

ii. **Diastolic heart failure** or diastolic dysfunction happens when the muscle in the left ventricle becomes stiff. Since it no longer relax, the heart can't quite fill with blood between beats.

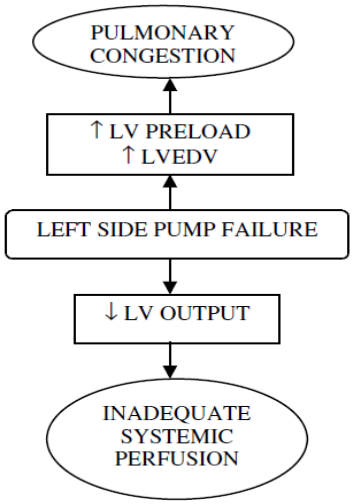

Figure 1: Consequences of left heart failure[5]

Right-Sided CCF

Right-sided CCF occurs when the right ventricle has difficulty pumping blood to the lungs. Blood backs up in the blood vessels, which causes fluid retention in the lower extremities, abdomen and other vital organs.[1]

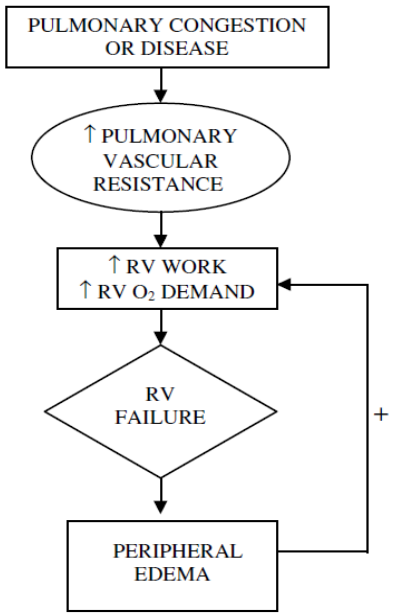

Figure 2: Consequences of right heart failure.[5]

It's possible to have left-sided and right-sided CCF at the same time. Often, one side of the heart starts to fail before the other. Usually, the disease starts in the left side and then travels to the right when left untreated.[1,4]

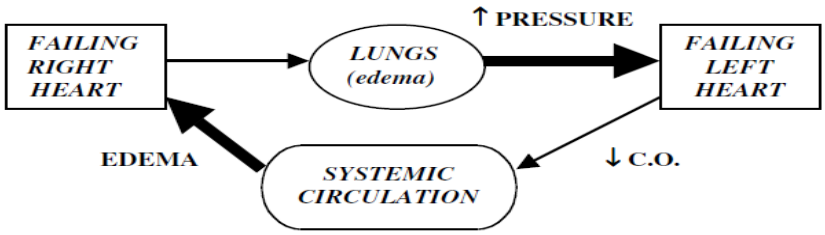

Figure 3: Circulation disturbance in heart failure.[5]

Stages Of CCF[1]

Table 1: Stages of CCF.

Stage	Main Symptoms
Class I	The patient doesn't experience any symptoms during typical physical activity
Class II	The patient is likely comfortable at rest, but normal physical activity may cause fatigue, palpitations and shortness of breath
Class III	The patient is likely comfortable at rest, but there is a noticeable limitation of physical activity. Even mild exercise may cause fatigue, palpitations and shortness of breath
Class IV	The patient is likely unable to carry on any amount of physical activity without symptoms, which are present even at rest

Causes of CCF

The mechanisms involved in CCF have been investigated from a variety of perspectives during the past half-century. These perspectives have sometimes been referred to as "models".[6] CCF may result from other health conditions that directly affect our cardiovascular system. Causes of CCF include coronary artery disease, congenital defects, long-term high blood pressure (hypertension), myocardial infarctions, and valve disorders.[1,4]

Coronary Artery Disease
Cholesterol and other types of fatty substances can block the coronary arteries, which are the small arteries that supply blood to the heart. This causes the arteries to become narrow. Narrower coronary arteries restrict the blood flow and can lead to damage in the arteries and ultimately leads to CCF.

Hypertension
When the blood pressure is higher than normal, it may lead to CCF. Hypertension occurs when the blood vessels become restricted by cholesterol and fat. This makes it harder for blood to pass through them.

Valve Conditions
The heart valves regulate blood flow through the heart by opening and closing to let blood in and out of the chambers. Valves that don't open and close correctly may force the ventricles to work harder to pump blood. This can be a result of a heart infection or defect.

Other Conditions
While heart related diseases can lead to CCF, there are other seemingly unrelated conditions that may increase the risk too. These include diabetes, thyroid disease and obesity. Severe infections and allergic reactions may also contribute to CCF.

Symptoms of CCF
In the early stages of CCF, most likely there won't be any noticeable change in the health. If the condition progresses, one experiences gradual changes in the body.

Table 2: Symptoms of CCF[1]

Symptoms that may be noticed first	Symptoms that indicate that the condition has worsened	Symptoms that indicate a severe heart condition
Fatigue	Irregular heart beat	Chest pain that radiates through the upper body
Swelling in the ankles, feet and legs	A cough that develops from congested lungs	Rapid breathing
Weight gain	Wheezing	Skin that appears blue, which is due to lack of oxygen in the lungs
Increased need to urinate, especially at night	Shortness of breath, which may indicate pulmonary edema	Fainting

Table 3: New York Heart Association Classification of Congestive Heart Failure.[7]

Stage/Degree	Symptoms and Activity-Limitations
I – None	No symptoms from ordinary activities
II – Mild	Comfortable at rest or during mild exertion
III – Moderate	Symptomatic with any activity
IV – Severe	Symptomatic at rest. Confined to bed or chair

Pathophysiology

Table 4: Pathophysiologic Changes Associated with Heart Failure.[8]

Pathophysiologic Changes Associated with Heart Failure	
Hemodynamic changes	**Cellular changes**
Decreased output (systolic dysfunction)	Inefficient intracellular Ca^{2+} handling
Decreased filling (diastolic dysfunction)	Adrenergic desensitization
	Myocyte hypertrophy
Neurohormonal changes	Reexpression of fetal phenotype proteins
Sympathetic system activation	Cell death (apoptosis)
Renin-angiotensin system activation	Fibrosis
Vasopressin release	
Cytokine release	

Physiologic Compensation for Heart Failure
The signs and symptoms of heart failure may not appear in the early stages as a result of a number of compensatory mechanisms that combine to maintain cardiac output. This early stage of heart failure is termed **compensated heart failure**. The compensatory responses are only effective in the short term and will eventually be unable to maintain cardiac output for a long period of time. **Decompensated heart failure** occurs when cardiac output is no longer adequately maintained and overt symptoms of heart failure appear.

Compensatory mechanisms include the following:

i. **Increased cardiac output** — The normal heart responds to increases in preload or LVEDV by increasing stroke volume and cardiac output. The more the heart is stretched by filling, the greater its responsive strength of contraction. With heart failure there are chronic increases in preload that continually distend the ventricular muscle fibers. Over time, the compensatory mechanism becomes ineffective because the cardiac muscle fibers stretch beyond the maximum limit for efficient contraction.

In addition, the oxygen requirements of the distended myocardium exceed oxygen delivery. At this point, further increases in preload are not matched by an increase in cardiac output.

ii. **Increased sympathetic activity** — The decrease in cardiac output that accompanies heart failure will lead to decreases in blood flow and blood pressure that activate the sympathetic nervous system. The result of sympathetic activation is an increase in circulating levels of catecholamines that cause peripheral vasoconstriction as well as an increase in heart rate and force of cardiac contraction (positive chronotropic and positive inotropic effects). Unfortunately, the failing myocardium becomes dependent on circulating levels of catecholamines to help it maintain cardiac output. Over time, the failing myocardium becomes less responsive to the stimulatory effects of these catecholamines and function continues to deteriorate.

iii. **Activation of renin–angiotensin system** — As a result of decreased cardiac output, blood flow to the kidneys will be significantly reduced. The kidneys respond to this reduction in blood flow by releasing the enzyme rennin. Renin ultimately leads to the production of angiotensin II in the plasma and the release of aldosterone from the adrenal gland. Angiotensin II is a powerful vasoconstrictor that increases systemic blood pressure while aldosterone acts on the kidney tubules to increase salt and water retention, a second factor that will increase systemic blood pressure. Other hormones that appear to be increasingly active during heart failure are antidiuretic hormone (ADH) from the pituitary gland and atrial natriuretic factor (ANF) that is released in response to atrial dilation. ANF may have a beneficial effect on CHF since it acts as a natural diuretic.

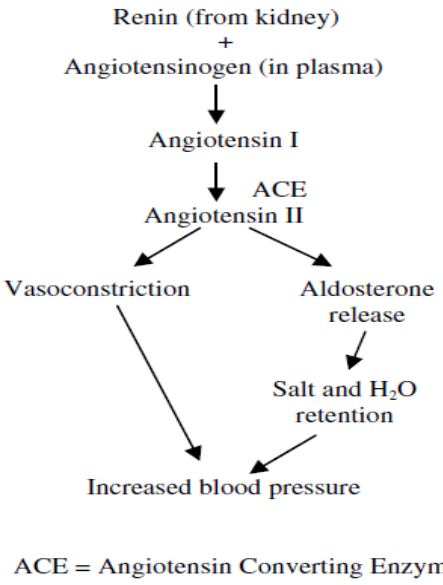

Figure 4: Consequences of rennin-angiotensin system activation in heart failure.[5]

iv. **Ventricular hypertrophy** — Faced with a chronic increase in workload, the myocardium responds by increasing its muscle mass. Although increased muscle mass can increase cardiac output in the short term, contractility eventually suffers as the metabolic demands of the hypertrophied myocardium continue to increase and the efficiency of contraction decreases[5].

Diagnosis of CCF

After reporting the symptoms to a doctor, they may refer the patient to a heart specialist, or cardiologist. The cardiologist will perform a physical exam. The exam may involve listening to the patient's heart with a stethoscope to detect abnormal heart rhythms. To confirm an initial diagnosis, the cardiologist might order certain diagnostic tests to examine the heart's valves, blood vessels and chambers.

Following are some tests the cardiologist may recommend

i. An **electrocardiogram** (EKG/ECG) records the heart's rhythm. Abnormalities in the heart's rhythm, such as a rapid heartbeat or irregular rhythm, could suggest that the walls of the heart's chamber are thicker than normal. That could be a warning sign for a heart attack.

ii. An **echocardiogram** uses sound waves to record the heart's structure and motion. The test can determine if there is already poor blood flow, muscle damage, or a heart muscle that doesn't contract normally.

iii. An **MRI** takes pictures of the heart. With both still and moving pictures, this allows the doctor to see if there is damage to the heart.

iv. **Stress tests** show how well a heart performs under different levels of stress. Making the heart work harder makes it easier for the doctor to diagnose problems.

v. **Blood tests** can check for abnormal blood cells and infections. Blood tests can also check the level of BNP, a hormone that rises with heart failure.

vi. **Cardiac catheterization** can show blockages of coronary arteries. The doctor will insert a small tube into the blood vessel and thread it from the upper thigh (groin area), arm or wrist. At the same time the doctor can take blood samples, use X-rays to view the coronary arteries and check blood flow and pressure in the heart chambers.[1]

Table 5: Modified Framingham Criteria for the Diagnosis of Chronic Heart Failure.[7]

Major Criteria	Minor Criteria
Neck-vein distention	Bilateral ankle edema
Orthopnea or paroxysmal nocturnal dyspnea	Night cough
Crackles (>10 cm above base of lung)	Dyspnea on exertion
Cardiomegaly on chest radiograph	Hepatomegaly
S_3 gallop	Pleural effusion
Central venous pressure >12 mm Hg	Tachycardia (>120 beats/min)
Left ventricular dysfunction on echocardiogram	
Weight loss >4.5 kg in response to CHF treatment	
Acute pulmonary edema	

Diagnosis of chronic heart failure (CHF) requires two of the major criteria or one of the major plus two of the minor criteria.

Treatment for CCF

Classification of Drugs for CCF[9]

1. Inotropic drugs

(a) Cardiac glycosides: Digoxin, Digitoxin, Ouabain
(b) Sympathomimetics: Dobutamine, Dopamine
(c) Phosphodiesterase III inhibitors: Amrinone (Inamrinone), Milrinone.

2. Diuretics

(a) High ceiling diuretics: Furosemide, Bumetanide.
(b) Thiazide like diuretics: Hydrochlorothiazide, Metolazone, Xipamide.

3. Inhibitors of Renin-Angiotensin system

(a) ACE-inhibitors: Enalapril, Ramipril and others.
(b) Angiotensin (AT1 receptor) antagonists: Losartan and others.

4. Vasodilators

(a) Venodilator: Glyceryl trinitrate and other nitrates.
(b) Arteriolar dilator: Hydralazine.
(c) Arteriolar + Venodilator: Sod. Nitroprusside.

5. β-Adrenergic blockers

Metoprolol, Bisoprolol, Carvedilol.

6. Aldosterone antagonist

Spironolactone, Eplerenone.

Rationale for Treatment of Heart Failure

Treatment for heart failure can be directed to reducing the workload on the failing heart and/or to enhancing cardiac contractility.

Treatment may include the following:

i. Restriction of physical activity to reduce cardiac workload.
ii. Reduction of preload through:
a. Salt and fluid restriction.
b. Venous dilation with vasodilator drugs.
c. The use of diuretic drugs to reduce fluid volume.
iii. Reduction of afterload through:
a. The use of arterial vasodilators.
b. The inhibition of angiotensin II formation by ACE inhibitor drugs.
iv. Blunting the effects of the catecholamines and adrenergic input with β-adrenergic receptor antagonists
v. Increasing contractility (positive inotropic agents):
a. Digitalis glycosides — digoxin.
b. Inhibitors of heart-specific phosphodiesterases — amrinone, milrinone.

With severe heart failure the last resort might be a heart transplant, although the current wait for transplant organs can be several years. Mechanical pumps called "left-ventricular assist devices" are currently available and can be used to take over a portion of the pumping function of the heart as a temporary measure. However, these mechanical assist devices are not designed as a long-term solution to heart failure. Considerable advances have been recently made in the development and implementation of self-contained mechanical hearts that are designed to be long-term replacements for the failing heart.

Drugs for Treatment of Heart Failure

i. Vasodilators

a. **Organic nitrates** — Dilate peripheral arteries and veins through relaxation of vascular smooth muscle; reduce preload and afterload on the heart. Postural hypotension, headache, peripheral edema, reflex tachycardia possible with nitrates.
b. **Arterial vasodilators** (example: prazosin) — Cause dilation of peripheral arteries by blockade of α_1-adrenoreceptors and reduce afterload.

ii. Diuretics

a. **Thiazide diuretics** (example: hydrochlorothiazide) — Act on distal convoluted tubules of kidney to decrease active sodium reabsorption and increase fluid excretion; They have moderate potency. Glucose intolerance, hypokalemia are associated with the use of thiazdes.
b. **Loop diuretics** (example: furosemide) — Powerful diuretics that inhibit the transport of sodium out of the ascending loop of Henle, leading to the loss of large volumes of sodium and fluids; Hypokalemia, metabolic alkalosis are common side effects associated with loop diuretics.

iii. β-Adrenergic Receptor Antagonists

Despite their potential for reducing cardiac output and force of contraction, numerous human studies have reported an improvement in symptoms, reduced hospitalization and decreased mortality in patients with heart failure receiving β-blocker therapy. The mechanism of their beneficial effect is unclear but may be related to blunted catecholamine effects, reduced risk of arrhythmia, myocardial remodeling or improved cardiac energetics.

iv. ACE Inhibitors (examples: Captopril, Enalapril)

Block the formation of angiotensin II and aldosterone thereby leading to a reduction in vascular resistance and reduced sodium/fluid retention. The common side effects of ACE inhibitors include hypotension, dry cough, possible renal failure in patients with renal artery stenosis.

v. Positive Inotropic Agents

a. Cardiac glycosides (digoxin, digitalis) — Increase force of cardiac contraction by increasing levels of intracellular calcium in cardiac muscle cells; Cardiac glycosides have narrow margin of therapeutic safety and their adverse effects include nausea, vomiting and arrhythmia. They have marked effects on cardiac conduction that may be useful for rapid atrial arrhythmias. They shows increased toxicity with reduced plasma K^+. They mainly undergoes renal elimination and may have increased half-life in elderly individuals or in patients with renal disease.

b. Other cardiotonic agents (dobutamine) — β_1-Adrenoreceptor agonist used for treatment of acute heart failure

c. Phosphodiesterase inhibitors (amrinone, milrinone) — Increases force of contraction through increased cAMP levels in cardiac cells.[5]

Drug utilization studies in Congestive cardiac failure (CCF) patients are the powerful exploratory tools to ascertain the role of drugs in the society. Hence periodical auditing of drug utilization pattern in CCF patients is vital for promotion of rational use of drugs, for increasing the therapeutic efficacy, cost effectiveness and for minimizing the adverse effects.[2]

CONCLUSION

Chronic heart failure is a complex cardiac condition that encompasses several etiologies and comorbidities. It arises in the differential diagnosis in all adult patients who present with dyspnea and/or respiratory failure. Definitive diagnosis is established by a careful history and physical examination and supportive laboratory data. A chest radiograph is useful in excluding a pulmonary etiology (eg, pneumonia); however, a spiral computed-tomography angiogram may be required if the diagnosis of pulmonary emboli is entertained. The availability of measuring serum brain natriuretic peptide and bedside echocardiography has aided in our diagnostic precision. Therapy is primarily directed toward normalizing the underlying physiologic changes with ACE inhibitors and slow titration of β-blockers. Diuretics are useful in reducing pulmonary vascular congestion, which may reduce or resolve dyspnea. Excessive therapy often reduces cardiac output or causes symptomatic hypotension, which occurs most commonly in patients with diastolic dysfunction. Treatment of the underlying etiology (silent ischemia or poorly controlled hypertension) may halt or slow the progression of the disease. Treatment of comorbidities (eg, underlying pulmonary disease, cigarette abuse, or diabetes) is essential in optimizing patient outcome and improving quality of life.

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CONFLICT OF INTEREST

We have no conflict of interest.

BIBLIOGRAPHY

1. Brindles Lee Macon and Kristeen Cherney. Congestive Heart Failure, 2015. https://www.healthline.com/health/congestive-heart-failure.
2. Bharath Kumar D., Chandrashekar R., Manohar V.R, Mohandas Rai et al. Drug Utilization Pattern in Patients with Congestive Cardiac Faiure in a South Indian Tertiary Care Hospital: A Retrospective Study. Int.Res.J.Pharm, 2015; 6(7): 463-466.
3. Prasanna Kumar B. Jewargi, Ravi D. Mala. Drug Utilization Study in Congestive Heart Failure at a Tertiary Care Hospital. Sch. J. App. Med. Sci., 2015; 3(2): 857-862.
4. Gerard J. Tortora, Sandra Reynolds Grabowski. The Cardiovascular System: The Heart. Principles of Anatomy and Physiology.10th edn. USA. John Wiley & Sons, Inc, 2003: 659-695.
5. Martin M. Zdanowicz. Essentials of Pathophysiology for Pharmacy. Washington, D.C. CRC Press LLC; 2002: 103-115.
6. Eugene Braunwald. Heart Failure. JACC: Heart Failure, 2013; 1(1): 1–20.
7. Michael S Figueroa, Jay I Peters. Congestive Heart Failure: Diagnosis, Pathophysiology, Therapy, and Implications for Respiratory Care. Respiratory Care, 2006; 51(4): 403-412.
8. Stephen J. McPhee, William F. Ganong. Pathophysiology of Disease: An Introduction to Clinical Medicine.5th edn. California, The McGraw-Hill Companies, 2006.
9. KD Tripathi. Pharmacological Classification of Drugs with Doses and Preparations. 4th edn. India. Jaypee Brothers Medical Publishers (P) Ltd., 2010; 71-72.