Review Article

Congestive Heart Failure: Epidemiology, Etiology, Pathophysiology and Neurohormonal Mechanism with Emerging Therapeutic Insights: A Review

Shivani.C.Lavate,* Sucheta.S.Pawar
Yashoda Technical Campus, College of Pharmacy, Satara, Dist- Satara Maharashtra, India
***Corresponding author's E-mail:** shivanilawate4356@gmail.com

Received: 06-03-2026; **Revised:** 18-05-2026; **Accepted:** 25-05-2026; **Published online:** 20-06-2026.

ABSTRACT

Heart failure (HF) has been considered a growing health problem since 1997 and continues to be a major health issue. This review examined research published since 2010 to better understand the prevalence of HF and its effects on different populations in the Middle East. Recent studies have shown that the number of new HF cases remains the same or even decreases slightly; however, deaths and hospitalizations due to HF have not improved significantly, even with better treatments. More people are now being diagnosed with a type of HF in which the heart's pumping strength is normal (preserved ejection fraction); however, there are still few proven treatments for this form. Significant variations exist in how HF impacts various demographics, particularly younger Black men and women, who generally experience poorer results. These trends emphasize the intricacy of heart failure (HF) and the difficulties tied to its management, especially in elderly patients who frequently have various health issues. Novel scientific methods, such as genetics and other "0mics" studies, might assist in uncovering the origins of HF and result in improved therapies. To genuinely diminish the effects of HF, the healthcare system needs to adopt a more comprehensive strategy that considers not just the heart but also the process of aging, various diseases, and social elements that influence health. Heart failure (HF) is a critical condition in which the heart struggles to pump blood effectively, leading to health complications and potential fatality. Despite improved treatments, numerous individuals still require hospitalization. The count of new cases remains steady, yet an increasing number of individuals are living with HF because of enhanced survival rates. A form known as HFpEF is on the rise, yet it has few treatment alternatives. HF can lead to swelling (edema) caused by fluid accumulation and hormonal changes in the body such as RAAS and ADH. Recent studies are concentrating on improved therapies and innovative strategies to address this condition.

Keywords: Heart Failure (HF), Congestive Heart Failure (CHF), Systolic dysfunction, Diastolic dysfunction, Respiratory Failure (RF).

1. Introduction

Congestive heart failure happens when the heart struggles to fill with blood or effectively pump it due to a structural or functional issue.

People with this condition often experience symptoms involving the heart and lungs, such as chest pain, a racing heartbeat, or difficulty breathing.[1]

Heart failure (HF) is not a single disease. Instead, it is a group of symptoms caused by various types of heart problems. Because HF has many causes and presents in different ways, it is harder to define than diseases that have a clear test for diagnosis, such as cancer; therefore, many different definitions of HF exist in medical books, research studies, and treatment guidelines. Some definitions focus on how the heart works, while others, such as the Framingham criteria, are mostly used for research.[2] The traditional definition states that HF is a condition in which the heart cannot pump enough blood for the body. Another definition describes it as a problem in the structure or function of the heart that prevents it from delivering sufficient oxygen to the body.[4] However, these definitions do not work well for all patients. For example, in one study of people with severe HF waiting for a heart pump, only 25% actually had low blood output at rest. This shows that older definitions do not fit most patients with HF adequately.[3] In everyday medical practice, other tools, such as blood tests for natriuretic peptides, are very helpful in diagnosing HF.[5]

Modern guidelines from organizations such as the ACC/AHA, HFA/ESC, and JHFS provide slightly different definitions; however, they all agree on a few key points.

1. HF is a clinical condition that consists of a range of symptoms and indicators.

2. Certain common symptoms need to be evident, including breathlessness, swelling from fluid accumulation, fatigue, or challenges with physical exertion.

3. There has to be a structural or functional issue with the heart, indicating that the heart is either impaired or not working correctly.

Heart failure is a condition in which the heart struggles to fill or pump blood effectively. It typically occurs as a result of other cardiac conditions. Numerous individuals globally are impacted, and treating it is also expensive. Medicines and medical devices have helped people live longer, but the disease often gets worse over time. In most cases, it cannot be completely cured.

2. Epidemiology

Heart failure is increasing worldwide because people are living longer and surviving other heart problems. In developed countries, new cases are stable, but in poorer regions, they are still high. A type called HFpEF now makes up about half of all cases. Death rates are still high, similar

to some cancers. Many patients are often re-hospitalized, which increases healthcare costs.

1. Types of Congestive Heart Failure:

HF is classified based on ejection fraction:

- Heart Failure with Reduced Ejection Fraction (HFrEF)
- Heart Failure with Preserved Ejection Fraction (HFpEF)
- Heart Failure with Mid-Range Ejection Fraction (HFmrEF)

Additionally, HF can be categorized as:

- Acute VS Chronic
- Left-sided VS Right-sided
- High-output VS Low-output HF

There are two main types of heart failure based on how well the left side of the heart pumps blood: heart failure with reduced ejection fraction (HFrEF) occurs when the heart's pumping ability is weak, usually with an ejection fraction below 40%. Heart failure with preserved ejection fraction (HFpEF) occurs when the heart pumps normally but is stiff and cannot relax properly; this is more common in women and in individuals with high blood pressure. HFpEF is usually defined as an ejection fraction of > 40–50%. A third category, heart failure with mid-range ejection fraction (HFmrEF), was added for patients whose ejection fraction fell between 40% and 50%, since they have features of both types.[1,2]

Left-Sided Heart Failure:

The left side of the heart receives oxygen-rich blood from the lungs and sends it to the rest of the body. The left ventricle is the main pumping chamber and performs most of the heart's work. When this part does not function well, the heart cannot pump blood as it should.

In left-sided heart failure, the left side of the heart must work harder to pump blood. Doctors measure the efficiency of the heart using ejection fraction (EF).[6] The normal EF is 55–60%.

There are two main types of such systems.

1. Systolic failure (HFrEF): The left ventricle cannot be squeezed properly. As a result, the heart cannot push enough blood out of the body. This is called heart failure with reduced ejection fraction, and the EF is ≤ 40 %.

2. Diastolic failure (HFpEF): The left ventricle becomes stiff and cannot relax normally. Because it cannot relax, it cannot fill with enough blood between heartbeats. This is called heart failure with preserved ejection fraction, and the EF is 50% or higher.

There is also a middle category called HFmrEF, where the EF is 41–49%. This type falls between the other two types.

Right-Sided Heart Failure: The right side of the heart pumps blood to the lungs to pick up oxygen. Right-sided heart failure usually occurs because the left side has already failed. When the left side does not pump well, pressure builds up in the lungs, making the right side work too hard. Eventually, the right side also weakens.[7] When this occurs, blood backs up in the veins, causing swelling.

Biventricular Heart Failure: This occurs when both the left and right sides of the heart fail. People may have symptoms from both sides, such as:

Shortness of breath (edema) Swelling in the body Feeling very tired or weak.

4. Etiology of Congestive Heart Failure:

4.1 Ischemic Heart Disease: The leading cause of HF, resulting from reduced blood supply to myocardium.

4.2 Valvular Heart Disease: Includes stenosis and regurgitation leading to volume or pressure overload.

4.3 Hypertension: Chronic pressure overload results in ventricular hypertrophy and dysfunction.

4.4 Cardiomyopathies: Dilated, Hypertrophic, Restrictive

4.5 Inflammatory Cardiomyopathy: Caused by infections, autoimmune conditions.

4.6 Infiltrative Cardiomyopathies: Includes amyloidosis and sarcoidosis.

4.7 Cardiac Amyloidosis: Protein deposition leading to stiff ventricles.

4.8 Takotsubo Cardiomyopathy: Stress-induced transient ventricular dysfunction.

4.9 Peripartum Cardiomyopathy: Occurs in late pregnancy or postpartum.

4.10 Obesity: Leads to increased cardiac workload and metabolic dysfunction.

4.11 Tachycardia and Arrhythmias: Persistent tachycardia can cause cardiomyopathy.

4.12 High-Output Heart Failure: Caused by conditions like anemia, hyperthyroidism.

5. Heart failure Etiologies:

Heart failure (HF) can occur for many reasons, but the most common cause is coronary artery disease (CAD), which reduces blood flow to the heart (ischemic heart disease). It is important for doctors to determine the exact cause so that they can choose the right treatment.

The causes of HF can be grouped into several categories, such as diseases of the heart muscle itself, conditions that cause abnormal substances to build up in the heart (infiltrative diseases), heart defects present at birth (congenital),problems with the heart valves, inflammation of the heart (myocarditis),high-output failure (when the body demands more blood flow than the heart can provide),and diseases that affect other parts of the body but also damage the heart.[1,3,5]

Approximately two-thirds of all HF cases are attributed to four major causes:

1. Ischemic heart disease (most common)
2. Chronic obstructive pulmonary disease (COPD)
3. Hypertensive heart disease (heart damage from long-term high blood pressure)
4. Rheumatic heart disease

Ischemic heart disease and COPD are more common in wealthier countries. In lower-income countries, heart failure is more often caused by high blood pressure, cardiomyopathy, rheumatic heart disease and myocarditis.[4,23,24]

Ischemic Heart Disease: Ischemic heart disease is the most common cause of heart failure worldwide. It occurs when the heart does not receive sufficient blood, which weakens the heart muscle and lowers the ejection fraction (EF). Cases are rising in developing countries as people adopt Western-style diets and lifestyles, and infections decrease with better medical care.

Valvular Heart Disease: Valvular heart disease is a common cause of heart failure. The most common cause of CHD in children and young adults worldwide is rheumatic heart disease, which occurs when the immune system reacts to a streptococcal infection and damages the heart valves, especially the mitral and aortic valves.[5] In adults, the main cause is age-related wear and tear, and the aortic valve is usually affected. Women more often have mitral valve problems (such as rheumatic disease or mitral valve prolapse), whereas men more often have aortic valve diseases (such as stenosis or regurgitation). Endocarditis, a valve infection, is also more common in men.[8]

Hypertension: High blood pressure can cause heart failure, even without blocked heart arteries. It places extra strain on the heart, making it work harder and causing the heart muscle to thicken. Hypertension is also associated with other conditions that lead to HF. Early and aggressive treatment of high blood pressure can significantly reduce the risk of developing heart failure. [3]

Cardiomyopathy: Cardiomyopathy refers to a group of heart muscle diseases in which the ventricles become enlarged or weak, not because of other problems, such as blocked arteries, valve disease, or high blood pressure. The main types are hypertrophic, dilated, restrictive, arrhythmogenic right ventricular and left ventricular non-compaction. Besides causing heart failure, cardiomyopathy can also lead to irregular heart rhythms or even sudden cardiac death, so finding the exact cause is very important. Many forms are genetic, so doctors take a detailed family history, especially if close relatives had sudden cardiac death after age 35. More than 50 genes can lead to dilated cardiomyopathy, and the symptoms can vary widely. Other factors, such as diabetes, toxins, or pregnancy, can also influence the disease. Rare conditions, such as Fabry disease, can cause heart failure by producing a hypertrophic cardiomyopathy pattern. [6,3,9]

Inflammatory Cardiomyopathy: Inflammatory cardiomyopathy occurs when the heart muscle becomes inflamed (myocarditis), leading to changes in the heart structure and poor heart function. The most common cause is a viral infection, while other causes include bacterial, fungal, or parasitic infections, toxic substances or drugs, and autoimmune diseases.[7]Chagas disease, caused by Trypanosoma cruzi in Latin America, often leads to myocarditis, cardiomyopathy, and heart failure (HF). Viruses such as adenovirus, entero-virus, herpes virus 6, Epstein–Barr virus, cytomegalovirus, HIV, hepatitis C, influenza A/B, and coronaviruses (including COVID-19) can also cause myocarditis.[10]

Infiltrative Cardiomyopathies: Infiltrative Cardiomyopathies In characterized by the accumulation of abnormal substances in the heart muscle. This makes the heart stiff, causing a restrictive pattern; the heart pumps normally, but it cannot relax and fill properly. [11-14]

Cardiac Amyloidosis: Misfolded proteins deposit in the heart, making it stiff and causing low blood pressure. These patients depend on good fluid levels for survival. Tafamidis is the only drug that can slow the disease, but it cannot reverse it and is very expensive.

Sarcoidosis: This condition forms inflammatory lumps (granulomas) in the heart, causing rhythm disturbances and conduction defects. Heart failure frequently occurs in individuals with diabetes mellitus. Beta-blockers must be used with care. Cardiac Hemochromatosis: Resulting from surplus iron in the heart. It begins as a limiting issue and eventually results in the deterioration of both heart sides. Patients exhibit sensitivity to low blood pressure; thus, standard heart failure treatments should be given with care.

Takotsubo (Stress-Induced) Cardiomyopathy: Often referred to as broken-heart syndrome, this condition is a transient type of heart failure where the left ventricle alters its shape and fails to pump effectively. It is not due to obstructed blood vessels. Potential reasons consist of coronary spasms, issues with small vessels, and stress-induced over activity of the nervous system. Management resembles that for typical heart failure, occasionally involving blood-thinning drugs if necessary.

Cases have become more common during the COVID-19 pandemic.[11,12]

Peripartum Cardiomyopathy: Peripartum cardiomyopathy is a type of heart failure that can occur late in pregnancy or within months after delivery. The heart's pumping function (LV systolic function) is reduced, causing symptoms of heart failure, and risk factors include older maternal age, Black race, multiple pregnancies, and possible genetic factors. If the heart wall motion is abnormal, blood thinners may be required because pregnancy increases the risk of clotting.

Recovery varies and is worse in women with very low heart function than in men.[13]

Obesity: Obesity is a major cause of heart failure in individuals under 40 years of age, responsible for up to 10% of cases.[15] It is often associated to HF with preserved ejection fraction (HFpEF). Fat tissue can release substances (like IL-1b, IL-8, and TNFα) that harm the heart and can reduce important heart-protective hormones called natriuretic peptides.[15,16]

Tachycardia and Arrhythmia: Tachycardia and Arrhythmia Fast heart rates (tachycardia) or irregular rhythms (arrhythmias) can cause heart failure by reducing the heart's pumping efficiency. The heart chambers may enlarge, and electrical changes occur in the heart cells. This triggers the typical heart failure response. Controlling the heart rate can often reverse these effects.[16]

High-Output Heart Failure: High-output heart failure occurs when the heart pumps a large amount of blood but still cannot meet the body's needs. Causes include thiamine (vitamin B1) deficiency, often in elderly, homeless, or alcohol-dependent people, as well as obesity, liver disease, and abnormal blood vessel connections. Thiamine deficiency reduces energy in heart cells and causes blood vessels to widen, forcing the heart to work harder, which can weaken it over time. Patients often have normal pumping function (EF), fluid Buildup in the lungs, high heart pressure, and elevated heart failure markers.[18,19]

5. Symptoms:

- Shortness of breath (especially during activity or lying down).
- Swelling in legs, ankles, or feet (edema).
- Fatigue and weakness.
- Rapid or irregular heartbeat.
- Persistent cough or wheezing (sometimes with white/pink mucus).
- Sudden weight gain due to fluid buildup.
- Difficulty in sleeping flat (need extra pillows).
- Reduced ability to exercise or do daily activities.

Dyspnea:

- One of the most common and troubling symptoms of heart failure is shortness of breath, also known as dyspnea.
- In heart failure, shortness of breath occurs because of problems involving both the heart and lungs.
- Initially, people experience shortness of breath during physical activity.
- This occurs because a weak heart cannot pump enough blood to meet the body's needs when a person is active.[20]
- When the heart cannot pump effectively, pressure builds up in the blood vessels of the lungs.
- This causes fluid to collect in the lungs (pulmonary congestion), making the lungs stiffer and more difficult to expand.
- Consequently, breathing becomes more difficult.[21]
- As heart failure worsens, shortness of breath can occur even while resting.
- This indicates more severe heart weakness (left ventricular dysfunction) and significant fluid accumulation in the lungs.
- Medical studies show that the worse the shortness of breath, the more fluid and pressure there usually is in the lungs and the left side of the lungs.[22]

Fatigue (Tiredness) in Heart Failure

- Fatigue is another common and exhausting symptom of heart failure.
- Individuals with heart failure often experience fatigue due to the following reasons:
- The heart cannot pump sufficient blood (low cardiac output).[23]
- This implies that the body's tissues and muscles do not receive sufficient oxygen.
- The muscles may weaken over time (muscle wasting or atrophy).[24]
- When muscles do not receive sufficient blood and oxygen, they switch to a backup energy system called anaerobic metabolism.
- This produces waste products that build up in the muscles and make people feel tired quickly.[25]

Two main approaches are used to reduce fatigue:

1. **Medications:** Drugs that improve heart function.
2. **Physical exercise/training:** Safe, supervised activity to strengthen the muscles and heart.

Both treatments have been shown to help patients with heart failure feel less tired.

Edema (Swelling) in Heart Failure

- In heart failure, edema refers to swelling, usually seen in the legs, feet, and stomach.
- This swelling occurs mainly because:

  When the right side of the heart becomes weak, it cannot pump blood effectively.
- This causes high pressure in the veins, and the extra pressure pushes the fluid out of the blood vessels into the surrounding tissues.[26]
- Another reason for swelling is that the body starts to retain excessive amounts of salt and water.

- This occurs because certain body systems (such as the renin-angiotensin-aldosterone system RAAS) become activated, causing the body to retain more fluid.
- The location of the swelling often depends on gravity:
- The legs and feet are usually the first to swell because they are the lowest parts of the body.[27]
- In more severe right-sided heart failure, fluid can accumulate in the abdomen, causing a swollen belly (ascites).

Orthopnoea and Paroxysmal Nocturnal Dyspnoea (PND)

- These are two breathing problems commonly observed in patients with congestive heart failure (CHF).

Orthopnea:

- Orthopnea refers to difficulty in breathing while lying down.
- When a person lies flat, the fluid in the body shifts toward the chest.
- This makes it difficult for the lungs to expand, causing shortness of breath.[28]

Paroxysmal Nocturnal Dyspnea (PND):

- The hallmark of PND is abrupt, intense dyspnea that awakens a person at night.
- The liquid from the legs returns to the circulatory system when the body is horizontal. This extra fluid increases blood flow back to the heart while you sleep, which raises lung pressure.
- Severe dyspnea, coughing, and choking symptoms result from this. People with orthopnea may prefer to sleep upright or use extra pillows.
- The symptoms usually go away as you sit up straight.
- These breathing issues are clear indicators of heart failure and aid medical professionals in distinguishing heart failure from other illnesses.[29]

6. Heart Failure Pathophysiology

Hormonal changes in the body and problems with blood circulation combine to create heart failure. The body tries to adapt by activating particular mechanisms to maintain blood circulation when the heart circulates less blood. These initially relieve the illness, but over time they worsen it by putting more strain on the heart.

7. Mechanisms behind the development of edema in CHF

Many people with heart failure (CHF) retain a lot of water and salt in their bodies. Certain bodily systems, such as the sympathetic nervous system, endothelins, ADH, and RAAS, become overactive.

In heart failure, various physiological mechanisms cause blood vessels to narrow and prompt the kidneys to retain sodium and water. On the other hand, the body also has protective systems—such as natriuretic peptides, nitric oxide, and prostaglandins—that promote the excretion of excess fluid. However, in heart failure conditions, these beneficial mechanisms are overwhelmed by the opposing ones, resulting in fluid retention and the development of edema. Additionally, many individuals with heart failure have impaired kidney function, which further reduces their ability to eliminate excess salt and water. [4,12,43]

Edema in HF results from:

- Increased hydrostatic pressure
- Sodium and water retention
- Reduced renal perfusion

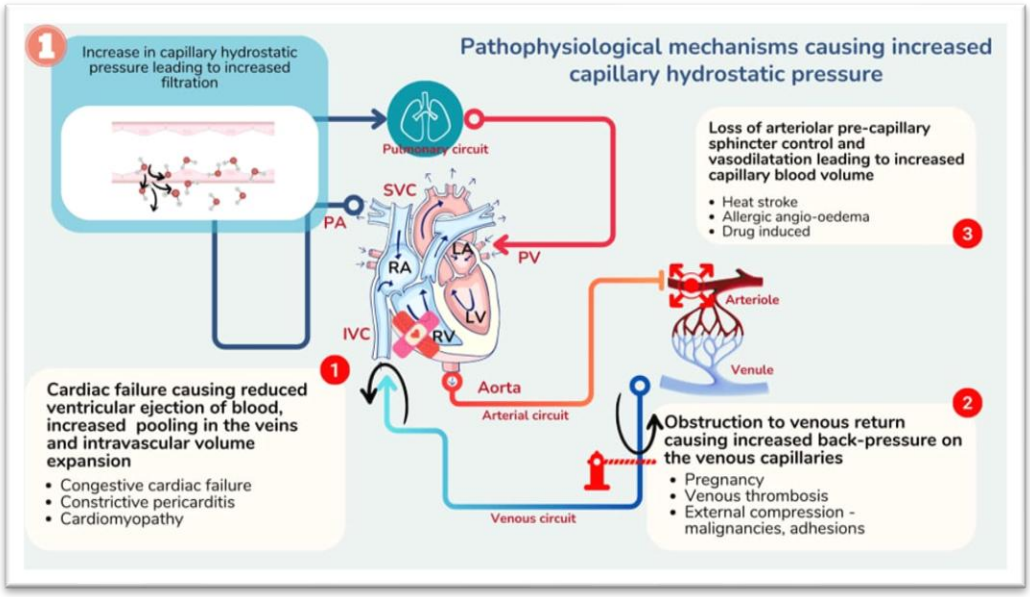

Figure 1: Mechanism of Edema Formation:

8. Neurohormonal systems

8.1 Vasoconstrictive / anti-natriuretic systems Renin-angiotensin-aldosterone system

The renin–angiotensin–aldosterone system (RAAS) is a hormone system that helps the body control blood pressure, sodium levels, and fluid balance in the body. It becomes active when the body is low on blood or pressure, such as during bleeding, dehydration, low salt intake, or increased sympathetic nervous system activity. Traditionally, the RAAS is known mainly for tightening blood vessels and helping the kidneys retain salt and water, which can raise blood pressure. When overactive, it can cause inflammation, oxidative stress, cell damage, and fibrosis, contributing to diseases such as hypertension, heart failure, and kidney damage. The system is initiated when the kidneys release renin, which produces angiotensin I, an inactive peptide. ACE found mostly in the lungs, converts angiotensin I into angiotensin II, a powerful active hormone that causes blood vessels to tighten and promotes salt and water retention by acting on AT1 receptors in the heart, kidneys, and blood vessels. Medications such as ACE inhibitors and ARBs block these harmful effects and protect the heart and kidneys. Aldosterone, another RAAS hormone, further increases sodium retention and can cause organ scarring, which is why aldosterone blockers are helpful. In recent years, researchers have discovered a second protective side of the RAAS. This pathway uses ACE2, which converts harmful Ang- II into Ang-(1–7), a peptide that relaxes blood vessels and reduces salt retention, inflammation, and fibrosis. ACE2 also converts Ang I into Ang-(1–9), which can become Ang-(1–7), and another enzyme, neprilysin, can also produce Ang-(1–7). This “depressor arm” of RAAS helps counterbalance the harmful effects of the traditional “pressor arm.”[43-55]

Angiotensin II (Ang- II) is a hormone that helps the body control blood pressure and fluid balance. It minimizes urine and salt elimination by constricting the kidneys' blood vessels, leading to reduced kidney blood circulation and lower sodium release. Ang- II also boosts nervous system activity, elevating heart output and blood pressure, and initiates the release of ADH, which aids the kidneys in retaining water. It further prompts thirst, leading to higher water consumption and an increase in blood volume. In heart failure, Ang- II concentrations rise excessively, leading the kidneys to retain more salt and water, aggravating fluid accumulation, partly via the release of aldosterone and endothelin. Medications like ACE inhibitors and ARBs inhibit Ang II and assist in eliminating excess sodium; nonetheless, they may also decrease renal blood flow and occasionally impair kidney function. ACE2 is a protein present in various organs, such as the heart and kidneys, that transforms Ang II into a protective compound known as Ang 1–7, which dilates blood vessels and mitigates inflammation and fibrosis. In heart failure, ACE2 activity rises to mitigate the detrimental effects of Ang II. In summary, Ang II is the detrimental, fluid-retaining element of the RAAS, while ACE2 and Ang 1–7 offer a protective counterbalance to its harmful impacts.[57-68]

Activated due to reduced renal perfusion.

- Renin converts angiotensinogen to angiotensin I
- ACE converts angiotensin I to angiotensin II
- Angiotensin II causes vasoconstriction and aldosterone release
- Aldosterone promotes sodium retention

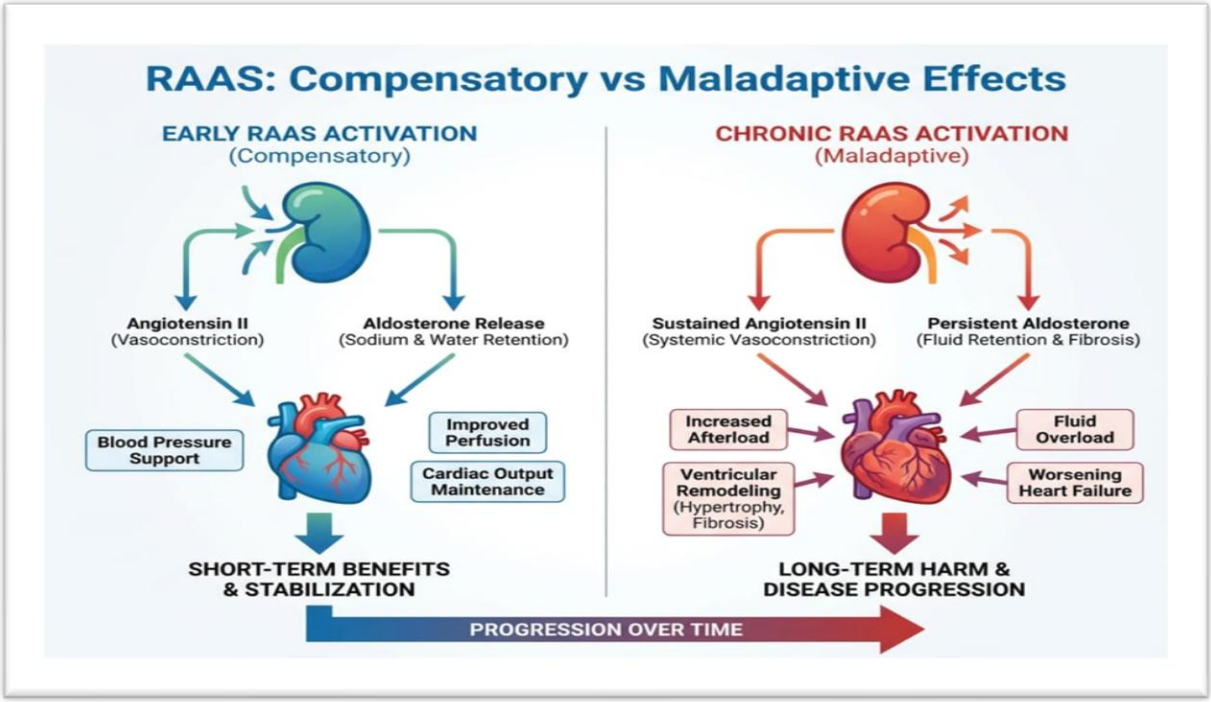

Figure 2: RAAS Pathway:

8.2 Sympathetic nervous system

The sympathetic nervous system sends signals through the renal (kidney) nerves, which affect the kidney blood vessels and parts of the kidney that make and filter urine. In early heart failure, these nerves become overactive, causing the body to release excessive norepinephrine (NE).[67]This initially helps maintain blood pressure; however, over time, it harms the heart and kidneys.[68] When the renal sympathetic nerves are overactive, the kidneys hold onto too much salt and water, reduce blood flow and filtration by tightening both the incoming and outgoing arterioles, and release more renin, which activates the RAAS and reduces the kidney's ability to get rid of salt.[69] Studies have shown that blocking or reducing these nerve signals through renal denervation or certain medication scan improve kidney blood flow and increase salt and water excretion, although some details are still debated. Overall, increased renal sympathetic nerve activity is a key reason why patients with advanced heart failure retain excess salt and water. [70-74]

Increases heart rate and contractility but leads to long-term damage.

8.3 Anti-diuretic hormone

Since the pioneering report by Szatalovicz et al. in the early 80s, several studies have reported elevated circulatory levels of ADH in patients with HF, especially in those with advanced CHF and hyponatremia. The increased secretion of ADH in these patients is attributed to non-osmotic stimuli, such as attenuated compliance of the left atrium and activation of the baroreceptors and RAAS.[76] This non-osmotic release of ADH is largely responsible for hyponatremia, a clinically important complication of heart failure, as ADH stimulates V2 receptors (V2) along with increased aquaporin-2 AQP 2 water channel density on the apical side of epithelial cells in the collecting duct, resulting in water retention and eventually hyponatremia. [77] The contribution of ADH to the excessive water balance in CHF is supported by the findings that oral treatment with V2 antagonists (aquaretics) provoked significant free water clearance, low urinary osmolarity, and elevation of plasma osmolality, along with down regulation of AQP-2 in the collecting duct. In addition to the activation of V2/AQP 2, ADH also stimulates V1a receptors localized to the vascular smooth muscle cells, with constriction of coronary vessels and stimulation of cardiac myocyte proliferation. These findings suggest an adverse role for vasopressin in fluid overload and cardiac re-modeling in patients with CHF. This notion is supported by clinical trials demonstrating that V2 blockade induces diuresis and lowers congestion without WRF when administered with furosemide to chronic HFrEF; however, unfortunately, it did not improve outcomes when applied during the post-acute phase. [78]

Promotes water retention and contributes to hyponatremia.

9. Emerging Therapeutic Insights:

Congestive Heart Failure (Emergency Management)

- **Oxygen Therapy:** Improves breathing
- **Diuretics:** Removes excess fluid (↓ edema, lung congestion)
- **Vasodilators:** Relax blood vessels (↓ heart workload)
- **Inotropes:** Increase heart pumping (severe cases)
- **Positioning:** Sitting position (easier breathing)
- **Fluid & Salt Restriction:** Prevents fluid buildup
- **Treat Underlying Cause:**
    a. Control BP
    b. Manage arrhythmia
    c. Treat infection

10. Future Directions

Future approaches in heart failure treatment are increasingly centered on precision medicine, which seeks to deliver tailored care based on a person's distinct biological characteristics. Progress in genomics enables scientists to analyze an individual's genetic composition, assisting in the identification of particular genes that could raise the likelihood of heart failure or affect how a patient reacts to specific medications. Likewise, proteomics consists of examining the proteins present in the body, which can offer insights into disease development and assist in discovering new biomarkers for early detection. Metabolomics, conversely, examines small molecules and metabolic alterations, providing greater insight into the impact of heart failure on body chemistry and energy consumption. By combining information from genomics, proteomics, and metabolomics, healthcare professionals can create more precise diagnostic instruments and targeted treatments. This method might assist in distinguishing heart failure subtypes, like HFpEF, and customizing treatment plans as needed. Precision medicine shows potential in forecasting disease advancement and averting complications through early intervention. Besides biological elements, tackling social determinants of health is crucial for enhancing outcomes in heart failure patients. Elements like income, education, healthcare access, nutrition, and living conditions greatly affect disease risk and management. Individuals from underprivileged backgrounds frequently experience prolonged diagnosis times, restricted access to advanced therapies, and increased hospitalization rates. Initiatives to mitigate these inequalities involve enhancing healthcare access, advocating for health education, and executing community-focused interventions. Policies in public health focused on minimizing risk factors such as hypertension, obesity, and unhealthy lifestyle choices are equally significant.

CONCLUSION

Heart failure remains a significant health issue impacting numerous individuals globally. It occurs when the heart fails to effectively pump blood, causing several complications. Despite advancements in treatments, it continues to result in significant rates of illness and mortality. Effective management is crucial for disease control and enhancing quality of life. Care should concentrate not just on the heart but also on other bodily systems impacted. Changes in lifestyle, medications, and consistent monitoring are crucial. Timely detection and appropriate treatment can enable patients to live longer and improve their quality of life.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Braunwald E. Heart failure. JACC Heart Fail. 2013;1:1-20.
2. Wagner, S · Cohn, K.Heart failure. A proposed definition and classification. Arch Intern Med. 1977; 137:675-678
3. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure. Circulation. 2013;128:e240-e327.
4. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2016;37:2129-2200.
5. Tsutsui H, Isobe M, Ito H, et al. JCS 2017/JHFS 2017 guideline on diagnosis and treatment of acute and chronic heart failure (digest version). Circ J. 2019;83:2084-2184.
6. McMurray JJ, Ostergren J, Pfeffer MA, Swedberg K, Granger CB, Yusuf S, et al. Clinical features and contemporary management of patients with low and preserved ejection fraction heart failure: baseline characteristics of patients in the CHARM programme.
7. Parshall MB, Schwartzstein RM, Adams L, et al. Update on mechanisms, assessment, and management of dyspnea. Am J Respir Crit Care Med. 2012;185:435-452.
8. Wenger NK. Current status of cardiac rehabilitation. J Am Coll Cardiol. 2008;51:1619-1631.
9. Noninvasive ventilation with bilevel positive airway pressure in heart failure patients. Hellenic J Cardiol. 2018;59:317-320.
10. Tu RH, Zeng ZY, Zhong GQ, et al. Exercise training and depression in heart failure: systematic review. Eur J Heart Fail. 2014;16:749-757.
11. von Haehling S, Anker SD. Cachexia in heart failure: update. J Cachexia Sarcopenia Muscle. 2014;5:261-263.
12. Whelton PK, Carey RM, Aronow WS, et al. 2018 guideline for high blood pressure in adults. Hypertension. 2018;71.
13. Gheorghiade M, Pang PS. Acute heart failure syndromes. J Am Coll Cardiol. 2009;53:557-573.
14. Katz AM, Zile MR. Molecular mechanisms in diastolic heart failure. Circulation. 2006;113:1922-1925
15. Sheer A, Heckman JE, Schneider EB, et al. CHF and COPD predict poor surgical outcomes. Dis Colon Rectum. 2011;54:1430-1437.
16. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for unstable angina. J Am Coll Cardiol. 2007;50:e1-e157.
17. Chaudhry SI, Wang Y, Concato J, et al. Weight change preceding hospitalization for heart failure. Circulation. 2007;116:1549-1554.
18. He FJ, Li J, MacGregor GA. Salt reduction and blood pressure. Cochrane Database Syst Rev. 2013
19. Ponikowski P, Voors AA, Anker SD, et al. ESC guidelines for heart failure.
20. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for heart failure. Circulation. 2022;145:e895-e1032.
21. CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe heart failure. N Engl J Med. 1987;316:1429-1435
22. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol. 2016;13:368-378.
23. Lind L, Ingelsson M, Sundstrom J, et al. Risk factors for cardiovascular diseases. Open Heart. 2021;8(2).
24. Noubiap JJ, Agbor VN, Bigna JJ, et al. Rheumatic heart disease prevalence. Sci Rep. 2019;9:17022.
25. Kim KH, Pereira NL. Genetics of cardiomyopathy. Korean Circ J. 2021;51:797-836.
26. Rezkalla SH, Kloner RA. Viral myocarditis. Trends Cardiovasc Med. 2021;31:163-169
27. Muchtar E, Blauwet LA, Gertz MA. Restrictive cardiomyopathy. Circ Res. 2017;121:819-837.
28. Brown KN, Pendela VS, Ahmed I, et al. Restrictive cardiomyopathy. StatPearls. 2023.
29. Matta AG, Carrié D. Takotsubo cardiomyopathy review. Med Sci Monit. 2023;29:e939020.
30. Bairashevskaia AV, Belogubova SY, Kondratiuk MR, et al. Takotsubo cardiomyopathy update. Int J Cardiol Heart Vasc. 2022;39:100990.
31. Ahmad SA, Brito D, Khalid N, et al. Takotsubo cardiomyopathy. StatPearls. 2023.
32. DeFilippis EM, Beale A, Martyn T, et al. Heart failure in women. Circ Res. 2022;130:436-454.
33. Wong CM, Hawkins NM, Jhund PS, et al. Young adults with heart failure: CHARM. J Am Coll Cardiol. 2013;62:1845-1854.
34. Volpe M, Gallo G. Obesity and cardiovascular disease. Front Cardiovasc Med. 2023;10:1136340.
35. Kim DY, Kim SH, Ryu KH. Tachycardia-induced cardiomyopathy. Korean Circ J. 2019;49:808-817.
36. Anakwue RC, Onwubere BJ, Anisiuba BC, et al. CHF in thyrotoxicosis. Vasc Health Risk Manag. 2010;6:473-477.
37. Schoenenberger AW, Schoenenberger-Berzins R, der Maur CA, et al. Thiamine in chronic heart failure. Clin Res Cardiol. 2012;101:159-164.
38. DiNicolantonio JJ, Liu J, O'Keefe JH. Thiamine and cardiovascular disease. Prog Cardiovasc Dis. 2018;61:27-32.
39. Reddy YNV, Melenovsky V, Redfield MM, et al. High-output heart failure. J Am Coll Cardiol. 2016;68:473-482.
40. Chayanupatkul M, Liangpunsakul S. Cirrhotic cardiomyopathy. Hepatol Int. 2014;8:308-315.
41. Abassi Z, Goltsman I, Karram T, Winaver J, Hoffman A. Aortocaval fistula in rat: a unique model of volume-overload congestive heart failure and cardiac hypertrophy. J Biomed Biotechnol. 2011;2011:729497.
42. Costanzo MR, Jessup M. Treatment of congestion in heart failure with diuretics and extracorporeal therapies: effects on symptoms, renal function, and prognosis. Heart Fail Rev. 2012;17:313-324.
43. Heywood JT, Fonarow GC, Costanzo MR, Mathur VS, Wigneswaran JR, Wynne J. High prevalence of renal dysfunction and its impact on

outcome in patients hospitalized with acute decompensated heart failure: ADHERE database. J Card Fail. 2007;13:422-430.

44. Ezekowitz J, McAlister FA, Humphries KH, Norris CM, Tonelli M, Ghali WA, et al. Association among renal insufficiency, pharmacotherapy, and outcomes in patients with heart failure and coronary artery disease. J Am Coll Cardiol. 2004;44:1587-1592.
45. Brewster UC, Setaro JF, Perazella MA. The renin-angiotensin-aldosterone system: cardiorenal effects and implications. Am J Med Sci. 2003;326:15-24.
46. Santos RAS, Oudit GY, Verano-Braga T, Canta G, Steckelings UM, Bader M. The renin-angiotensin system: beyond classical paradigms. Am J Physiol Heart Circ Physiol. 2019;316:H958-H970.
47. Basso N, Terragno NA. History of the renin-angiotensin system. Hypertension. 2001;38:1246-1249.
48. Sharma N, Anders HJ, Gaikwad AB. Renin-angiotensin system in acute kidney injury. Biomed Pharmacother. 2019;110:764-774.
49. Forrester SJ, Booz GW, Sigmund CD, Coffman TM, Kawai T, Rizzo V, et al. Angiotensin II signal transduction: mechanisms of physiology and pathophysiology. Physiol Rev. 2018;98:1627-1738.
50. Tigerstedt R, Bergman PQ. Niere und kreislauf. Skand Arch Physiol. 1898;8:223-271.
51. Danser AHJ, Saris JJ, Schuijt MP, van Kats JP. Is there a local renin-angiotensin system in the heart? Cardiovasc Res. 1999;44:252-265.
52. Sullivan RD, Mehta RM, Tripathi R, Reed GL, Gladysheva IP. Renin activity in heart failure with reduced systolic function. Int J Mol Sci. 2019;20:3182.
53. Pieruzzi F, Abassi ZA, Keiser HR. Expression of renin-angiotensin system components in experimental heart failure. Circulation. 1995;92:3105-3112.
54. Silver SA, Beaubien-Souligny W, Shah PS, Harel S, Blum D, Kishibe T, et al. Prevalence of acute kidney injury in COVID-19 patients: systematic review. Kidney Med. 2021;3:83-98.e1.
55. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2001;345:861-869.
56. Santos RAS, Ferreira AJ, Simões E, Silva AC. Advances in ACE2–Ang(1-7)–Mas axis. Exp Physiol. 2008;93:519-527.
57. Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. N Engl J Med. 1999;341:577-585.
58. Myers BD, Deen WM, Brenner BM. Effects of norepinephrine and angiotensin II on renal function. Circ Res. 1975;37:101-110.
59. Schoolwerth AC, Sica DA, Ballermann BJ, Wilcox CS. Renal considerations in ACE inhibitor therapy. Circulation. 2001;104:1985-1991.
60. Sica DA. Edema mechanisms in the patient with heart failure and treatment options. Heart Fail Clin. 2008;4:511–8. doi:10.1016/j.hfc.2008.04.002
61. Beldhuis IE, Streng KW, Ter Maaten JM, Voors AA, van der Meer P, Rossignol P, et al. Renin-angiotensin system inhibition, worsening renal function, and outcome in heart failure patients with reduced and preserved ejection fraction: a meta-analysis of published study data. Circ Heart Fail. 2017;10:e003588. doi:10.1161/CIRCHEARTFAILURE.116.003588
62. Abassi Z, Assady S, Khoury EE, Heyman SN. Letter to the editor: angiotensin converting enzyme 2: an ally or a Trojan horse? Implications to SARS-CoV-2 related cardiovascular complications. Am J Physiol Heart Circ Physiol. 2020;318:H1080–3. doi:10.1152/ajpheart.00215.2020
63. Lee VCH, Lloyd EN, Dearden HC, Wong K. A systematic review to investigate whether angiotensin-(1-7) is a promising therapeutic target in human heart failure. Int J Pept. 2013;2013:260346. doi:10.1155/2013/260346
64. Tripathi R, Sullivan RD, Fan T-HM, Mehta RM, Gladysheva IP, Reed GL. A low-sodium diet boosts Ang (1-7) production and NO-cGMP bioavailability to reduce edema and enhance survival in experimental heart failure. Int J Mol Sci. 2021;22:4035. doi:10.3390/ijms22084035
65. DiBona GF, Kopp UC. Neural control of renal function. Physiol Rev. 1997;77:75–197. doi:10.1152/physrev.1997.77.1.75
66. Denton KM, Luff SE, Shweta A, Anderson WP. Differential neural control of glomerular ultrafiltration. Clin Exp Pharmacol Physiol. 2004;31:380–6. doi:10.1111/j.1440-1681.2004.04002.x
67. Kaye D, Esler M. Sympathetic neuronal regulation of the heart in aging and heart failure. Cardiovasc Res. 2005;66:256–64. doi:10.1016/j.cardiores.2005.02.012
68. Watson AMD, Hood SG, May CN. Mechanisms of sympathetic activation in heart failure. Clin Exp Pharmacol Physiol. 2006;33:1269–74. doi:10.1111/j.1440-1681.2006.04523.x
69. DiBona GF. Peripheral and central interactions between the renin angiotensin system and the renal sympathetic nerves in control of renal function. Ann N Y Acad Sci. 2001;940:395–406. doi:10.1111/j.1749-6632.2001.tb03693.x
70. Kon V, Yared A, Ichikawa I. Role of renal sympathetic nerves in mediating hypoperfusion of renal cortical microcirculation in experimental congestive heart failure and acute extracellular fluid volume depletion. J Clin Invest. 1985;76:1913–20. doi:10.1172/JCI112187
71. Dupont AG. Effects of carvedilol on renal function. Eur J Clin Pharmacol. 1990;38(Suppl 2):S96–100. doi:10.1007/BF01409473
72. Heitmann M, Davidsen U, Stokholm KH, Rasmussen K, Burchardt H, Petersen EB. Renal and cardiac function during alpha1-beta-blockade in congestive heart failure. Scand J Clin Lab Invest. 2002;62:97–104. doi:10.1080/003655102753611717
73. Chen HH, Schrier RW. Pathophysiology of volume overload in acute heart failure syndromes. Am J Med. 2006;119:S11–6. doi:10.1016/j.amjmed.2006.09.012
74. Szatalowicz VL, Arnold PE, Chaimovitz C, Bichet D, Berl T, Schrier RW. Radioimmunoassay of plasma arginine vasopressin in hyponatremic patients with congestive heart failure. N Engl J Med. 1981;305:263–6. doi:10.1056/NEJM198107303050506
75. Schrier RW. Role of diminished renal function in cardiovascular mortality: marker or pathogenetic factor? J Am Coll Cardiol. 2006;47:1–8. doi:10.1016/j.jacc.2005.07.067
76. Noda Y, Sasaki S. Updates and perspectives on aquaporin-2 and water balance disorders. Int J Mol Sci. 2021;22:12950. doi:10.3390/ijms222312950
77. Goldsmith SR. Arginine vasopressin antagonism in heart failure: current status and possible new directions. J Cardiol. 2019;74:49–52. doi:10.1016/j.jjcc.2019.03.001
78. Cohn JN. The management of chronic heart failure. N Engl J Med. 1996;335:490–8.