

## *Heart Failure: Causes, Symptoms, and Management Strategies*

### **Abstract**

Cardiac failure (HF) is a multifaceted clinical center described by the incapacity of a heart to sufficiently pump blood leading to inefficient perfusion of tissues. It has two main categories that are represented by ejection fraction: Heart Failure with Reduced Ejection Fraction (HFrEF), or Heart Failure with Preserved Ejection Fraction (HFpEF). The following review is a summary of research on the diverse causes, symptoms as well as management approaches involved in heart failure. Heart disorder comes about as a result of the following factors: coronary artery disease, hypertension, cardiomyopathy, valvular heart diseases, arrhythmias, and congenital heart defects the main symptoms include shortness of breath, weariness/tiredness, and swelling of the feet among others. Management strategies cover lifestyle modifications, medicines using treatment (e.g. diuretics, ACE inhibitors, beta-blockers), and further treatments like cardiac resynchronization therapy (CRT) consisting of implantable cardioverter defibrillators (ICDs) along with mechanical circulatory support (MCS); however, there is also heart transplant aside them. Future progression in genetic treatment gene therapy, as well as stem cell study, sounds promising over improving results obtained from HF treatment.

### **Introduction**

The inability of the heart to pump blood effectively to meet the metabolic needs of the body characterizes heart failure. There is a clinical syndrome that is complex and develops because of structural or functional deficiencies in ventricular filling and ejection of blood [1]. Based on ejection fraction, HF is usually separated into two major types; HFpEF, in which the proportion is preserved, and HFrEF, where it is diminished. Heart Failure with Reduced Ejection Fraction commonly referred to as systolic heart failure, is the condition where patients experience a weakened heart muscle that fails to contract forcefully. Similarly, Heart failure with preserved ejection fraction is also called diastolic heart failure and it describes a heart muscle that has become stiff and noncompliant such that it lacks proper relaxation during filling [2].

Heart failure is very important when it comes to public health. It results in many deaths and illnesses internationally, affecting around 26 million individuals. In the US, 6 million people are affected by this disease and 1 million hospitalization cases are attributed to this condition [3]. The problem is placed on healthcare systems because repeated admissions to hospitals are expensive, complex medical treatments are required for a long time, and advanced therapies must be carried out. This also means that there are more elderly people who suffer from diseases like high blood pressure, diabetes, and obesity, leading to an increased incidence rate of heart failure [4].

This article reviews the current information on the causes, symptoms, and treatment of heart failure with a focus on recent inroads and remaining hurdles. It intends to consolidate current research that is new as well as clinical guidelines to improve comprehension about the disease condition and show the way for future management and cure directions.

## **Causes of Heart Failure**

### ***Coronary Artery Disease (CAD)***

Coronary artery disease (CAD) is still the major cause of heart failure (HF) all over the world. CAD is a condition where there is a buildup of fat deposits in the arteries of the heart muscle thus limiting blood supply to this area. The underlying process involves injury to the endothelium, accumulation of fats, inflammatory responses, and plaque development occasionally complicated by thrombus growth following rupture [5]. Significance of CAD in HF Development Myocardial ischemia and infarction causes cardiomyocyte loss, myocardial fibrosis, and consequent ventricular remodeling, with dilation and hypertrophy within this remodeling compensating for the initially lost contractile function yet culminating in systolic dysfunction and HF [6]. The research revealed that the likelihood of getting heart failure among CAD patients is higher than myocardial infarction serving as a crucial cause for HF [7].

### ***Hypertension***

Older people are at a higher risk of heart failure due to hypertension. When the blood pressure rises chronically, it forces the left ventricle to pump against an increased resistance thereby causing a condition known as left ventricular hypertrophy (LVH). Yet with time, this state can

turn out to be quite harmful – it requires more oxygen from the heart muscles, they become stiff and their relaxing ability is impaired leading to diastolic dysfunction as well as heart failure with preserved ejection fraction (HFpEF) [8]. In demonstrating the substantial association of hypertension to HF, the Framingham Heart Study showed that hypertension is markedly associated with both HFpEF and HFrEF increase in risk substantially [9]. **Factors that affect hypertension-related HF prevalence differ by population including killing Black Americans and fucking old people because of social status issues of those who care how they lived physically [10]. mind the language**

### ***Cardiomyopathy***

Cardiomyopathy includes several diseases that affect the heart muscle; these can be grouped under three headings: dilated cardiomyopathy, hypertrophic cardiomyopathy, and restrictive cardiomyopathy. Dilated cardiomyopathy features ventricular enlargement and depressed systolic function, often having an unknown cause however can have an etiology like viral infections, alcoholism, and chemotherapy among others [11]. Hypertrophic Cardiomyopathy (HCM) is characterized by an asymmetrical growth of the ventricles, mainly the septum, causing an impediment to outflow and poor diastolic performance. HCM is often inherited, resulting from changes in sarcomeric proteins [12]. An uncommon type of heart disease called restrictive cardiomyopathy makes it difficult for the heart to expand properly because its walls become stiff during filling; it is typically associated with diseases that infiltrate muscle between cells, such as amyloidosis or sarcoidosis [13]. Such illnesses lead to heart failure (HF) by reducing the ability of the heart pumps to eject blood into the rest of body parts (cardiac output), irregular heart rhythms (arrhythmias), and swelling.

### ***Valvular Heart Disease***

HF often has valvular heart disease underlying it. Such conditions can include aortic stenosis, mitral regurgitation, and mitral stenosis. Nishimura & Otto [14] point out that if not treated, it may evolve into LVH and subsequently HFCLVD due to increased afterload triggered by aortic stenosis. On the other hand, when the mitral valve leaks, it causes congestive heart failure by overloading ventricles thus leading to systolic dysfunction in the left ventricle of the human heart. Both conditions disrupt the normal functioning of the heart leading to heart failure. To

prevent valvular heart disease from progressing to heart failure, one must go for surgical interventions such as valve replacement or repair [15].

### ***Arrhythmias***

HF is affected by arrhythmias significantly, with atrial fibrillation (AF) being a particularly notable contributor. Efficient ventricular filling is compromised by fast, abnormal atrial contractions in AF that therefore decrease the amount of blood that is pumped by the heart. According to January et al., [16] if it persists over time this may lead to cardiomyopathy due to the overworking of the heart which causes it to dilate and lose its strength. For example, research like the AFFIRM trial has shown that AF management is important for preventing HF. This highlights the necessity of maintaining heart rate by controlling it or using **rhythmograms** [17].

### ***Congenital Heart Disease***

Congenital heart disease (CHD) refers to heart defects that are present at birth and include ventricular septal defects (VSD), atrial septal defects (ASD), and tetralogy of Fallot. These alterations in normal blood flow due to the defects can cause increased effort for the heart muscle, leading to heart failure when not managed early. There have been significant improvements in survival rates and long-term outcomes for people with CHD due to advances in pediatric cardiology, yet some still run the risk of HF development later in life after residual cardiac enzyme deficiencies or other surgical interventions' effects [18][19].

### ***Other Causes***

Infections, endocrine disorders, and toxins are other factors that can cause HF. Viral infections usually make the heart muscles inflamed hence leading to myocarditis (acute HF) and sometimes cardiomyopathy which will be chronic [20]. In addition, among the diseases causing heart failure are endocrine disorders including diabetes mellitus and hyperthyroidism. Myocardial fibrosis with dysfunction is a feature of diabetic cardiomyopathy while diabetes mellitus may accelerate atherosclerosis according to Kenny and Abel [21]. Increased metabolic demand and heart rate possibly lead to HF through hyperthyroidism. This is worsened by toxic cardiomyopathy that comes after myocardial damage caused directly by toxins such as alcohol, and chemotherapy drugs among others. [22] [23].

## **Symptoms of Heart Failure**

### ***Dyspnea***

One of the most notable as well as disturbing symptoms of heart failure (HF) is feeling short of breath also known as dyspnea. Various factors are responsible for this dyspnea in cases of HF and they include heart as well as lung factors. Initially, dyspnea is present during exertion (hardly breathing while working) due to a decrease in cardiac output that would have otherwise permitted an increase in the heart's ability to raise its total workload [24]. The reduced cardiac output results in higher pulmonary capillary pressures which lead to increased pulmonary congestion as well as a reduction in lung compliance. With the progression of HF, dyspnea may be present at rest indicating an advanced state of left ventricular dysfunction accompanied by significant pulmonary congestion [25]. It is well documented in clinical literature that the increasing severity of dyspnea parallels the extent of pulmonary congestion and left atrial pressure [26].

### ***Fatigue***

Tiredness is yet another usual and weakening sign for HF. There are complex reasons for fatigue associated with HF: these are greatly reduced cardiac output, bad oxygen delivery to the peripheral tissues, and muscle atrophy [27]. Diminished blood flow to the skeletal muscles results in the early onset of anaerobic metabolism leading to the build-up of metabolic waste products that cause fatigue feeling. There is an identification of two different strategies for improving heart function among people with heart failure; these strategies include pharmacological management as well as physical training, which both have been shown to reduce tiredness among patients suffering from heart failure [27] [28].

### ***Edema***

Edema in HF is characterized by engorgement primarily around the legs, feet, and tummy region, which results from excessive venous pressure raised by the failure of the right ventricle that forces filtration across intercellular gaps [29]. Retention of sodium and water, which is mediated by neurohormonal factors such as the activation of the Renin-Angiotensin-Aldosterone (RAAS) system, contributes to more fluid accumulation [30]. The localization of edema varies with

gravity causing peripheral edema commonly noted in lower limbs as a result of gravity while ascites ( abdominal edema) occurs in more advanced cases characterized by severe right-sided HF [31].

### ***Orthopnea and Paroxysmal Nocturnal Dyspnea***

Orthopnea is what causes someone to feel short of breath in a lying down position, whereas paroxysmal nocturnal dyspnea (PND) complicated with sudden breathlessness at night is a symptom worth noting as it suggests a person has congestive heart failure (CHF). It leads to pulmonary congestion since it results from the gravitation of fluid from the legs into the chest cavity once the person goes to bed, thus increasing capillary pressure (Lung sounds EMST Resources). During sleep, Paroxysmal Nocturnal Dyspnea is considered to occur gradually due to interstitial fluid reabsorption into the circulation, leading to an acute rise in preload and pulmonary congestion [32]. These clinical symptoms differentiate heart failure patients from others [33].

### ***Cough and Wheezing***

In chronic congestive heart failure (CHF), diagnosis can be difficult because typical symptoms (like cough or wheezing) mimic those seen in many respiratory diseases, such as chronic obstructive pulmonary disease (COPD) or asthma. A dry unproductive cough is usually observed due to pulmonary congestion and edema irritating the airways [34]. Heart failure patients commonly have heart failure manifestations due to left ventricular systolic or diastolic dysfunction, and the presence of weakness, confusion, and impaired concentration usually indicate multiorgan involvement [35]. In such syndromes, the principal adaptive response is neurohormonal activation with consequent vasoconstriction, water retention, and increased heart rate [36].

### ***Weight Gain***

Weight gain in people with heart failure is often a sign of fluid accumulation and progression of the disease. Observing changes in body mass is significant in recognizing decompensations early and may also benefit modifying therapy [37]. A rapid increase in weight is usually considered when an individual increases more than 2-3 pounds in a day, or 5 pounds per week; this points

out to an excess accumulation of fluid that needs urgent medical attention to avoid any worsening [38]. Weighing yourself regularly and learning about how to spot swelling at the beginning of congestive heart failure are important in self-care for patients with the condition [39].

## **Management Strategies for Heart Failure**

### **Lifestyle Modifications**

Effectively managing Heart Failure (HF) involves a holistic approach that includes lifestyle adjustments which greatly help to control symptoms and improve life quality.

#### ***Dietary Changes***

HF patients must have dietary changes chiefly noting a low sodium eating regimen for maintenance and recovery. Consuming high levels of sodium worsens fluid retention which in turn negatively affects the situation of persons suffering from heart failure like edema and dyspnea [40]. For such a group of people, the American Heart Association [41] however recommends a maximum of 1500mg/day as opposed to more than 2300 mg per day. Monitoring fluid intake is crucial—overconsumption spells volume overdose. In the case of advanced HF, patients are usually counseled to limit their intake of fluids to amounts ranging between 1.5 and 2 liters per day [42].

#### ***Physical Activity***

For patients with HF, cardiovascular fitness and overall heart health improve with regular exercise. A study by Taylor et al., (2014) has suggested that practicing aerobics contributes to the quality of life as it is related to minimal hospitalization cases due to affectionate failure. In the trial known as HF-ACTION, it was shown that supervised exercise training was able to lead to substantial growth in peak oxygen uptake with lower chances of death or being hospitalized for patients with HF. (O'Connor et al., 2009). The present recommendation on doing exercises is very subjective depending on a patient's health status but generally requires moderate aerobics should be done over 20/30mins per, 3-5 times or more per week [43].

#### ***Smoking Cessation and Alcohol Limitation***

One ought to cease smoking for the sake of managing heart failure, this is because smoking leads to poor endothelial functioning and, an increase in oxidation stress and inflammation hence making the situation more critical [44]. It is indicated that stopping smoking diminishes the chance of fresh myocardial attack and consequent heart failure which is illustrated well in the study by INTERHEART [45]. It is important to restrict alcohol intake because it can cause a heart condition called cardiomyopathy and may make heart failure symptoms worse. It is recommended by The European Society of Cardiology that women should have no more than one drink in a day and men two [46]

### **Pharmacological Treatments**

The management of heart failure must always involve drug therapy which aims at reducing symptoms, leading to less hospital admission, and prolonging lifespan.

#### ***Diuretics***

Diuretics are frequently utilized to handle liquid collecting in HF. Loop diuretics for example furosemide show efficacy when it comes to the reduction of edema and pulmonary congestion since they also induce sodium as well as water excretion (Mullens et al., 2009). In some resistant cases, thiazide diuretics can be incorporated into treatment for further diuretic effects [47]. Research strongly indicates that in HF patients diuretic therapy causes symptom reduction and enhanced exercise tolerance [48].

#### ***ACE Inhibitors/ARBs***

Angiotensin-converting enzyme (ACE) inhibitors as well as angiotensin receptor blockers (ARBs) are important when treating HF with reduced ejection fraction (HFrEF). Thus, they help in reducing vasoconstriction and sodium retention amongst other adverse effects of renin-angiotensin-aldosterone system (RAAS) thereby decreasing afterload as well as preload [48]. Packer et al. [49] showed a significant decrease in mortality and hospitalization when patients took ACE inhibitors, as shown in CONSENSUS and SOLVD studies. For those who cannot tolerate this kind of medication other options such as ARBs were approved, because they have similar effects; such studies are found in the CHARM trial too [50].

### ***Beta-blockers***

It is essential to use beta-blockers for managing HF because they fight the harmful consequences of long-term activation of sympathetic nerve fibers such as tachycardia and elevation of oxygen consumption by the heart muscle [51]. There have been several important researches on this issue including MERIT-HF and COPERNICUS which testified that using some other types like metoprolol and carvedilol decreases the chances of death and hospitalization among HFREF sufferers [49].

### ***Mineralocorticoid Receptor Antagonists (MRAs)***

Mineralocorticoid receptor antagonists (MRAs), such as spironolactone and eplerenone, have been shown to help control heart failure by blocking the aldosterone hormone that causes water and salt retention as well as heart muscle stiffening. The studies by [52] pointed out that RALES and EMPHASIS-HF tests resulted in notable decreases in death and hospitalization rates among patients who got the same treatment with these medications. MRAs are particularly beneficial in patients with advanced HF and those with HFpEF [53].

### ***ARNI (Angiotensin Receptor-Nepriylsin Inhibitors)***

In HF management, angiotensin receptor-nepriylsin inhibitors (ARNIs) are a novel category of drugs. Compared to enalapril, the study demonstrated that sacubitril/valsartan had a considerable effect on cardiovascular death as well as HF hospitalizations. By inhibiting both the RAAS as well as nepriylsin, ARNIs allow for an increase in urinary sodium excretion, vasodilatation, and a decrease in heart remodeling [50].

## **Advanced Therapies for Heart Failure**

### ***Cardiac Resynchronization Therapy (CRT)***

Cardiac Resynchronization Therapy (MRT) is seen as a very important way of helping people who have serious heart problems (HF) and a problem with their heartbeat. This was proved by a very important COMPANION study in which many people were helped with CRT as well as good treatment for their disease [54]. CRT is designed to enhance cardiac synchronization by electrically stimulating the left and right ventricles together, resulting in improved ventricular contraction producing a decrease in desynchrony. Not only does CRT help to relieve way of life

symptoms, but there is also evidence that it may work on exercise capacity improvements as well LV function [lv function] parameters such as quality of life parameters [lv function] [55]. CRT is indicated for symptomatic HF with reduced ejection fraction (HFrEF), left bundle branch block, and evidence of ventricular desynchrony on electrocardiogram (ECG) [1]. Even though it has changed the management of HF, CRT still presents various challenges such as patient selection, device optimization, and non-responder rates; this implies that further studies need to be done as well as continuous improvement of its strategies.

### ***Implantable Cardioverter-Defibrillators (ICDs)***

To prevent sudden cardiac death (SCD) in patients with severe ventricular arrhythmias, this calls for the placement of implantable cardioverter-defibrillators (ICDs). The efficiency of reducing mortality among HF patients who have a low ejection fraction has been clinically validated using the MADIT-II trial and SCD-HeFT study [56][57]. Implantable cardioverter defibrillators (ICDs) constantly observe the rhythm of the heart and dispatch shock waves or pacing treatments in case there are dangerous arrhythmias, thus stopping what could have been fatal arrhythmic episodes. It is advised by guidelines that individuals who have HF together with heart murmur cannot pump blood effectively should be implanted with ICDs for prevention against future risk [58]. Despite its efficacy in lowering mortality, issues such as device-related complications, inappropriate shocks, and cost-effectiveness continue to require regular evaluation and refinement to ensure patients are selected appropriately

### ***Mechanical Circulatory Support (MCS)***

Devices that provide mechanical support include for example left ventricular assist devices (LVAD) among others that are advanced therapies that have led to revolutionizing the management of end-stage HF because they offer failing heart some support mechanically via LVAD and this enhances hemodynamics as well as end-organ perfusion. In patients with advanced HF not eligible for heart transplantation, the REMATCH landmark trial revealed a meaningful increase in survival with the help of LVAD therapy as compared to optimal medical therapy alone [59]. Subsequent changes in the design of LVADs have resulted in devices that are smaller in size while maintaining improved durability due to continuous-flow mechanization leading to fewer incidences of complications like stroke or infection [60]. The life expectancy of

individuals with advanced HF has been enhanced greatly by LVAD treatment. However, it comes with many challenges such as complications caused by device usage, side effects, and a lifetime requirement for anticoagulation. To further enhance HF treatment and reach more patients through MCS, some modern technologies like fully implantable devices and percutaneous MCS options have been introduced which seems to offer hope.

### ***Heart Transplantation***

Some patients with end-stage HF do not respond to medications or devices and in this case, heart transplantation can be the best treatment. Guidelines from the International Society for Heart and Lung Transplantation (ISHLT) are used by doctors to decide who should get this surgery namely those with severe symptoms no matter how much medical help they get nor how many devices have been prescribed plus no other important illnesses along with emotional fitness according to Khush et al. [61]. According to Khush et al. [61], the one-year survival rate surpasses 90% with outstanding long-term survival and lifestyle. However, there are significant challenges in heart transplantation due to the few organ donors available, perioperative risks, and lifelong immunosuppressive medicine use. Outcomes in heart transplants have significantly improved and the potential list of candidates has grown large due to Major strides in organ preservation, selection of donors, and anti-rejection drug therapies.

### **Emerging Therapies**

#### ***Gene Therapy***

This research shows that gene therapy can be used as a new way of treating heart failure by targeting those molecular causes as well as mutations causing such disease [62]. Preclinical studies have shown that gene therapy can enhance heart function, stop reverse remodeling, and promote the recovery of myocardium [62]. Nowadays research is mapping strategies for transferring genes, optimizing vectors, and editing target genes in the treatment of genetic mutations related to HF phenotypes and family cardiomyopathies. There is still much that needs to be done in terms of study on immune reactions vector safety off-target to apply this way genetically permanently.

#### ***Stem Cell Therapy***

In HF, stem cell therapy is a promising approach for healing and revitalizing the myocardium. Preclinical and initial-phase clinical studies have demonstrated that different types of stem cells such as mesenchymal stem cells and cardiac progenitor cells can enhance heart function, induce angiogenesis, and decrease scar formation [63]. The role of stem cells is to release factors that control inflammation, stimulate tissue recovery, and improve endogenous heart repair processes. The problems faced by stem cells in therapy encompass the identification of the optimal source of cells, how to deliver cells, their engraftment degree, and lasting security. Current research aims at improving treatment through stem cell techniques, such as cell manipulation, tissue production, and combined treatments, to increase therapeutic efficiency and clinical transference in HF.

## **Conclusion**

Heart failure is a common and intricate medical syndrome originating from multiple structural and functional abnormalities of the heart resulting in inadequate ejection and filling of blood. This condition is caused mainly by coronary artery disease, hypertension, cardiomyopathy, valvular heart disease, arrhythmias, and congenital heart defects and presents with symptoms such as dyspnea, fatigue, and edema. The treatment for heart failure consists of lifestyle changes, drugs used medicinally, and advanced therapies like CRT, ICDs, MCS, and heart transplants. While substantial progress has been achieved, it is believed that future developments in the treatment and control of heart failure can happen as a result of continuous research on gene-related therapies including stem cell therapy.

## References

1. Ponikowski P, Voors AA, Anker SD, et al.: 2016 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *European Heart Journal*. 2016, 37:2129–200. <https://doi.org/10.1093/eurheartj/ehw128>
2. Green GB: Heart Failure and the Emergency Department: Epidemiology, Characteristics, and Outcomes. *Heart Failure Clinics*. 2009, 5:1–7. <https://doi.org/10.1016/j.hfc.2008.08.001>
3. Heidenreich PA, Albert NM, Allen LA, et al.: Forecasting the Impact of Heart Failure in the United States: A Policy Statement From the American Heart Association. *Circulation: Heart Failure*. 2013, 6:606–19. <https://doi.org/10.1161/hhf.0b013e318291329a>
4. Riegel B, Moser DK, Buck HG, et al.: Self-Care for the Prevention and Management of Cardiovascular Disease and Stroke. *Journal of the American Heart Association*. 2017, 6: <https://doi.org/10.1161/jaha.117.006997>
5. Libby P, Ridker PM, Maseri A: Inflammation and Atherosclerosis. *Circulation*. 2002, 105:1135–43. <https://doi.org/10.1161/hc0902.104353>
6. Pfeffer MA, Braunwald E: Ventricular remodeling after myocardial infarction. Experimental observations and clinical implications. *Circulation*. 1990, 81:1161–72. <https://doi.org/10.1161/01.cir.81.4.1161>
7. Gerber Y, Weston SA, Redfield MM, et al.: A Contemporary Appraisal of the Heart Failure Epidemic in Olmsted County, Minnesota, 2000 to 2010. *JAMA Internal Medicine*. 2015, 175:996. <https://doi.org/10.1001/jamainternmed.2015.0924>
8. Vasan RS: The Role of Hypertension in the Pathogenesis of Heart Failure. *Archives of Internal Medicine*. 1996, 156:1789. <https://doi.org/10.1001/archinte.1996.00440150033003>
9. Levy D: The progression from hypertension to congestive heart failure. *JAMA: The Journal of the American Medical Association*. 1996, 275:1557–62. <https://doi.org/10.1001/jama.275.20.1557>
10. Carnethon MR, Pu J, Howard G, et al.: Cardiovascular Health in African Americans: A Scientific Statement From the American Heart Association. *Circulation*. 2017, 136: <https://doi.org/10.1161/cir.0000000000000534>

11. Hershberger RE, Cowan J, Jordan E, Kinnamon DD: The Complex and Diverse Genetic Architecture of Dilated Cardiomyopathy. *Circulation Research*. 2021, 128:1514–32. <https://doi.org/10.1161/circresaha.121.318157>
12. Maron BJ, Maron MS: Hypertrophic cardiomyopathy. *The Lancet*. 2013, 381:242–55. [https://doi.org/10.1016/s0140-6736\(12\)60397-3](https://doi.org/10.1016/s0140-6736(12)60397-3)
13. Paller MS, Martin CM, Pierpont ME: Restrictive cardiomyopathy: an unusual phenotype of a lamin A variant. *ESC Heart Failure*. 2018, 5:724–6. <https://doi.org/10.1002/ehf2.12294>
14. Nishimura RA, Otto CM, Bonow RO, et al.: 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. *Journal of the American College of Cardiology*. 2014, 63:e57–185. <https://doi.org/10.1016/j.jacc.2014.02.536>
15. Valvular Heart Disease. *Indian Heart Journal*. 2012, 64:S5–13. <https://doi.org/10.1016/j.ihj.2012.10.018>
16. January CT, Wann LS, Alpert JS, et al.: 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. *Circulation*. 2014, 130: <https://doi.org/10.1161/cir.0000000000000041>
17. Olshansky B, Rosenfeld LE, Warner AL: The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. Approaches to control rate in atrial fibrillation. *ACC Current Journal Review*. 2004, 13:50. <https://doi.org/10.1016/j.accreview.2004.06.035>
18. Hoffman JIE, Kaplan S: The incidence of congenital heart disease. *Journal of the American College of Cardiology*. 2002, 39:1890–900. [https://doi.org/10.1016/s0735-1097\(02\)01886-7](https://doi.org/10.1016/s0735-1097(02)01886-7)
19. Moodie D: The Journal Congenital Heart Disease-2016. *Congenital Heart Disease*. 2016, 11:5–6. <https://doi.org/10.1111/chd.12342>
20. Shintaku M, Uchiyama K, Kobayashi Y: Chronic myocarditis with a long clinical course: Report of an autopsy case of probable autoimmune myocarditis. *Pathology International*. 2017, 67:521–5. <https://doi.org/10.1111/pin.12568>
21. Mechanisms underlying heart failure in type 2 diabetes mellitus. *Heart and Metabolism*. 2019, 37–9. <https://doi.org/10.31887/hm.2019.80/hbugger>

22. Guzzo-Merello G: Alcoholic cardiomyopathy. *World Journal of Cardiology*. 2014, 6:771. <https://doi.org/10.4330/wjc.v6.i8.771>
23. Yeh ETH, Bickford CL: Cardiovascular Complications of Cancer Therapy: Incidence, Pathogenesis, Diagnosis, and Management. *Journal of the American College of Cardiology*. 2009, 53:2231–47. <https://doi.org/10.1016/j.jacc.2009.02.050>
24. Parshall MB, Schwartzstein RM, Adams L, et al.: An Official American Thoracic Society Statement: Update on the Mechanisms, Assessment, and Management of Dyspnea. *American Journal of Respiratory and Critical Care Medicine*. 2012, 185:435–52. <https://doi.org/10.1164/rccm.201111-2042st>
25. Wenger NK: Current Status of Cardiac Rehabilitation. *Journal of the American College of Cardiology*. 2008, 51:1619–31. <https://doi.org/10.1016/j.jacc.2008.01.030>
26. Effects of noninvasive ventilation with bilevel positive airway pressure on exercise tolerance and dyspnea in heart failure patients. *Hellenic Journal of Cardiology*. 2018, 59:317–20. <https://doi.org/10.1016/j.hjc.2017.11.005>
27. Tu R-H, Zeng Z-Y, Zhong G-Q, et al.: Effects of exercise training on depression in patients with heart failure: a systematic review and meta-analysis of randomized controlled trials. *European Journal of Heart Failure*. 2014, 16:749–57. <https://doi.org/10.1002/ejhf.101>
28. von Haehling S, Anker SD: Prevalence, incidence and clinical impact of cachexia: facts and numbers-update 2014. *Journal of Cachexia, Sarcopenia and Muscle*. 2014, 5:261–3. <https://doi.org/10.1007/s13539-014-0164-8>
29. Zile MR, Baicu CF, Gaasch WH: Diastolic Heart Failure — Abnormalities in Active Relaxation and Passive Stiffness of the Left Ventricle. *New England Journal of Medicine*. 2004, 350:1953–9. <https://doi.org/10.1056/nejmoa032566>
30. Whelton PK, Carey RM, Aronow WS, et al.: 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018, 71: <https://doi.org/10.1161/hyp.0000000000000065>

31. Gheorghide M, Pang PS: Acute Heart Failure Syndromes. *Journal of the American College of Cardiology*. 2009, 53:557–73. <https://doi.org/10.1016/j.jacc.2008.10.041>
32. Katz AM, Zile MR: New Molecular Mechanism in Diastolic Heart Failure. *Circulation*. 2006, 113:1922–5. <https://doi.org/10.1161/circulationaha.106.620765>
33. 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction: Executive Summary: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Catheterization and Cardiovascular Interventions*. 2013, 82:E1–27. <https://doi.org/10.1002/ccd.24776>
34. Sheer A, Heckman JE, Schneider EB, Wu AW, Segal JB, Feinberg R, Lidor AO: Congestive Heart Failure and Chronic Obstructive Pulmonary Disease Predict Poor Surgical Outcomes in Older Adults Undergoing Elective Diverticulitis Surgery. *Diseases of The Colon & Rectum*. 2011, 54:1430–7. <https://doi.org/10.1097/dcr.0b013e31822c4e85>
35. Chaouat A, Bugnet A-S, Kadaoui N, et al.: Severe Pulmonary Hypertension and Chronic Obstructive Pulmonary Disease. *American Journal of Respiratory and Critical Care Medicine*. 2005, 172:189–94. <https://doi.org/10.1164/rccm.200401-006oc>
36. Anderson JL, Adams CD, Antman EM, et al.: ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction. *Journal of the American College of Cardiology*. 2007, 50:e1–157. <https://doi.org/10.1016/j.jacc.2007.02.013>
37. Chaudhry SI, Wang Y, Concato J, Gill TM, Krumholz HM: Patterns of Weight Change Preceding Hospitalization for Heart Failure. *Circulation*. 2007, 116:1549–54. <https://doi.org/10.1161/CIRCULATIONAHA.107.690768>
38. Cheitlin MD: Effects of Oral Tolvaptan in Patients Hospitalized for Worsening Heart Failure: The EVEREST Outcome Trial. *Yearbook of Cardiology*. 2008, 2008:386–8. [https://doi.org/10.1016/s0145-4145\(08\)01029-0](https://doi.org/10.1016/s0145-4145(08)01029-0)
39. McDonagh TA, Metra M, Adamo M, et al.: 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *European Heart Journal*. 2021, 42:3599–726. <https://doi.org/10.1093/eurheartj/ehab368>

40. He FJ, Li J, MacGregor GA: Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database of Systematic Reviews*. Published Online First: 30 April 2013. <https://doi.org/10.1002/14651858.cd004937.pub2>
41. Eckel RH, Jakicic JM, Ard JD, et al.: 2013 AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk. *Circulation*. 2013, 129:S76–99. <https://doi.org/10.1161/01.cir.0000437740.48606.d1>
42. Seferović PM: ESC/HFA Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2016. *Journal of Cardiac Failure*. 2017, 23:S7. <https://doi.org/10.1016/j.cardfail.2017.08.005>
43. Taylor RS, Sagar VA, Davies EJ, et al.: Exercise-based rehabilitation for heart failure. *Cochrane Database of Systematic Reviews*. Published Online First: 27 April 2014. <https://doi.org/10.1002/14651858.cd003331.pub4>
44. Lonn E, Bosch J, Teo KK, Pais P, Xavier D, Yusuf S: The Polypill in the Prevention of Cardiovascular Diseases. *Circulation*. 2010, 122:2078–88. <https://doi.org/10.1161/circulationaha.109.873232>
45. Yusuf S, Hawken S, Ounpuu S: Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *ACC Current Journal Review*. 2004, 13:15–6. <https://doi.org/10.1016/j.accreview.2004.11.072>
46. Mullens W, Abrahams Z, Francis GS, et al.: Importance of Venous Congestion for Worsening of Renal Function in Advanced Decompensated Heart Failure. *Journal of the American College of Cardiology*. 2009, 53:589–96. <https://doi.org/10.1016/j.jacc.2008.05.068>
47. Yancy CW, Jessup M, Bozkurt B, et al.: 2013 ACCF/AHA Guideline for the Management of Heart Failure. *Journal of the American College of Cardiology*. 2013, 62:e147–239. <https://doi.org/10.1016/j.jacc.2013.05.019>
48. McMurray JJV, Packer M, Desai AS, et al.: Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. *New England Journal of Medicine*. 2014, 371:993–1004. <https://doi.org/10.1056/nejmoa1409077>
49. Packer M, Bristow MR, Cohn JN, Colucci WS, Fowler MB, Gilbert EM, Shusterman NH: The Effect of Carvedilol on Morbidity and Mortality in Patients with Chronic Heart

- Failure. *New England Journal of Medicine*. 1996, 334:1349–55. <https://doi.org/10.1056/nejm199605233342101>
50. McMurray JJ, Östergren J, Swedberg K, et al.: Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *The Lancet*. 2003, 362:767–71. [https://doi.org/10.1016/s0140-6736\(03\)14283-3](https://doi.org/10.1016/s0140-6736(03)14283-3)
51. Bristow MR, Gilbert EM, Abraham WT, et al.: Carvedilol Produces Dose-Related Improvements in Left Ventricular Function and Survival in Subjects With Chronic Heart Failure. *Circulation*. 1996, 94:2807–16. <https://doi.org/10.1161/01.cir.94.11.2807>
52. Correction to: Prognostic Value of Albuminuria and Influence of Spironolactone in Heart Failure With Preserved Ejection Fraction: The TOPCAT Trial. *Circulation: Heart Failure*. 2018, 11: <https://doi.org/10.1161/hhf.0000000000000031>
53. Lyakishev AAL: Angiotensin–Neprilysin Inhibition Versus Enalapril in Heart Failure. *Kardiologija*. 2014, 12\_2014:47–8. <https://doi.org/10.18565/cardio.2014.12.47-48>
54. Bristow MR, Saxon LA, Boehmer J, et al.: Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure. *New England Journal of Medicine*. 2004, 350:2140–50. <https://doi.org/10.1056/nejmoa032423>
55. Linde C, Gold MR, Abraham WT, St John Sutton M, Ghio S, Cerkevnik J, Daubert C: Long-term impact of cardiac resynchronization therapy in mild heart failure: 5-year results from the REsynchronization reVERses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study. *European Heart Journal*. 2013, 34:2592–9. <https://doi.org/10.1093/eurheartj/eh160>
56. Bardy GH, Lee KL, Mark DB, et al.: Amiodarone or an Implantable Cardioverter–Defibrillator for Congestive Heart Failure. *New England Journal of Medicine*. 2005, 352:225–37. <https://doi.org/10.1056/nejmoa043399>
57. Prophylactic Implantation of a Defibrillator in Patients with Myocardial Infarction and Reduced Ejection Fraction. *Survey of Anesthesiology*. 2003, 47:73. <https://doi.org/10.1097/00132586-200304000-00009>
58. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al.: 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. *Circulation*. 2018, 138: <https://doi.org/10.1161/cir.0000000000000549>

59. Rose EA, Gelijns AC, Moskowitz AJ, et al.: Long-term use of a left ventricular assist device for end-stage heart failure. *The New England journal of medicine*. 2001, 345:1435–43. <https://doi.org/10.1056/NEJMoa012175>
60. Kirklin JK, Pagani FD, Kormos RL, et al.: Eighth annual INTERMACS report: Special focus on framing the impact of adverse events. *The Journal of Heart and Lung Transplantation: The Official Publication of the International Society for Heart Transplantation*. 2017, 36:1080–6. <https://doi.org/10.1016/j.healun.2017.07.005>
61. Khush KK, Cherikh WS, Chambers DC, et al.: The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-sixth adult heart transplantation report — 2019; focus theme: Donor and recipient size match. *The Journal of Heart and Lung Transplantation*. 2019, 38:1056–66. <https://doi.org/10.1016/j.healun.2019.08.004>
62. Fernández-Ruiz I: Targeting factor XIa. *Nature Reviews Cardiology*. 2016, 13:632–2. <https://doi.org/10.1038/nrcardio.2016.154>
63. Nair N, Gongora E: Stem cell therapy in heart failure: Where do we stand today? *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*. 2020, 1866:165489. <https://doi.org/10.1016/j.bbadis.2019.06.003>