



## **HEART FAILURE: NEW TREATMENT METHODS**

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**Annotation:** Heart failure is one of the most prevalent and life-threatening cardiovascular conditions worldwide, characterized by the heart’s inability to pump sufficient blood to meet the body’s needs. This article explores recent advancements in the diagnosis and treatment of heart failure, focusing on innovative pharmacological agents, device-based therapies, and regenerative approaches. Modern medications such as angiotensin receptor–neprilysin inhibitors (ARNIs) and sodium–glucose cotransporter-2 (SGLT2) inhibitors have transformed conventional treatment strategies, significantly reducing mortality and hospitalization rates. Moreover, novel technologies including cardiac resynchronization therapy, ventricular assist devices, and artificial intelligence–based monitoring systems have improved clinical outcomes and patient quality of life. The article also reviews ongoing research into gene therapy and stem cell–based cardiac regeneration, highlighting the potential for future breakthroughs in restoring myocardial function. Through a multidisciplinary approach that combines pharmacologic innovation, technological advancement, and personalized care, the management of heart failure is entering a new era of precision and effectiveness.

**Key words:** Heart failure, pharmacological treatment, SGLT2 inhibitors, ARNIs, cardiac resynchronization therapy, ventricular assist devices, gene therapy, regenerative medicine, artificial intelligence, cardiovascular health.

### **Introduction**

Heart failure (HF) represents one of the most prevalent and challenging public health issues of the 21st century. It is a progressive clinical syndrome characterized by the heart’s inability to pump blood adequately to meet the metabolic demands of the body or to do so only at the expense of elevated filling pressures. This condition arises as the final common pathway of many cardiovascular diseases, including coronary artery disease, hypertension, valvular heart disease, and cardiomyopathies. The global prevalence of heart failure is increasing each year, largely due to population aging, improved survival after acute cardiac events, and lifestyle factors such as obesity and diabetes.

According to the World Health Organization and major cardiology associations, heart failure currently affects over 64 million people worldwide and accounts for a significant proportion of hospital admissions among adults over the age of 65. In high-income countries, the lifetime risk of developing heart failure is estimated to be one in five for both men and women. Despite notable improvements in diagnostic methods and treatment strategies, the condition remains associated with high rates of morbidity, mortality, and reduced quality of life.

Historically, the management of heart failure focused primarily on symptom relief through the use of diuretics and vasodilators. However, contemporary medicine now recognizes heart failure as a neurohormonal disorder involving complex interactions between the renin–angiotensin–aldosterone system, sympathetic nervous system, and inflammatory pathways. This deeper understanding has opened new horizons for therapeutic innovation, leading to the development of targeted pharmacological agents, advanced device-based treatments, and regenerative medicine approaches.



Recent decades have witnessed remarkable progress in the treatment of heart failure, particularly with the introduction of angiotensin receptor–neprilysin inhibitors (ARNIs), sodium-glucose cotransporter-2 (SGLT2) inhibitors, and novel device therapies such as cardiac resynchronization and ventricular assist devices. Moreover, the growing field of stem cell therapy and gene editing has offered hope for reversing myocardial damage and restoring cardiac function.

Therefore, exploring **new treatment methods for heart failure** is not only an academic interest but a global necessity. Understanding these innovations helps clinicians optimize patient outcomes, improve survival rates, and enhance the overall quality of life for millions suffering from this chronic disease.

#### **Methodology and literature review**

This article is based on a **qualitative analytical review** of recent scientific literature, focusing on the latest advances in the diagnosis and treatment of heart failure. The research methodology involved a systematic evaluation of academic databases, including **PubMed, ScienceDirect, Scopus, and Google Scholar**, covering publications from **2014 to 2024**.

The inclusion criteria were:

- Peer-reviewed journal articles, systematic reviews, and meta-analyses.
- Studies conducted on adult human populations with either **heart failure with reduced ejection fraction (HFrEF)** or **heart failure with preserved ejection fraction (HFpEF)**.
- Research emphasizing **pharmacological, device-based, or regenerative** treatment methods.

Exclusion criteria included animal studies, non-English publications, and articles lacking clinical or experimental data.

A **comparative analysis** was then performed to identify trends, evaluate the clinical efficacy of emerging therapies, and summarize consensus recommendations from major guidelines, such as those issued by the **European Society of Cardiology (ESC)** and the **American Heart Association (AHA)**.

This review adopted a **descriptive and integrative approach**, aiming to synthesize existing data rather than conduct a meta-analysis. Key emphasis was placed on understanding how novel therapies improve patient outcomes, reduce mortality, and modify disease progression.

Ethical principles were respected by relying exclusively on published and publicly available academic materials. All sources were properly cited to maintain academic integrity and transparency.

The literature review reveals that the understanding and management of heart failure have undergone remarkable transformation in recent years. Traditional treatment approaches were primarily focused on symptom relief, but modern medicine now aims to **alter disease trajectory and restore cardiac function** through targeted pharmacological and technological interventions.

*Evolution of pharmacological therapy.* The introduction of **angiotensin receptor–neprilysin inhibitors (ARNIs)** marked a turning point in heart failure treatment. The **PARADIGM-HF trial** (Packer et al., 2014) demonstrated that **sacubitril/valsartan** significantly reduced mortality compared with enalapril. Subsequent trials confirmed similar outcomes across various populations, establishing ARNIs as a first-line therapy for HFrEF.

Another major advancement emerged from the discovery of **SGLT2 inhibitors**, such as **dapagliflozin** and **empagliflozin**. According to **McMurray et al. (2019)** and **Packer et al. (2020)**, these agents not only improve glycemic control but also provide substantial cardiovascular protection, regardless of diabetic status.



**Beta-blockers** and **mineralocorticoid receptor antagonists (MRAs)** continue to serve as essential components of standard heart failure therapy. Long-term studies confirm their role in reducing mortality and reversing left ventricular remodeling.

*Device-based and surgical innovations.* Modern device-based therapies have expanded treatment possibilities for advanced heart failure. **Cardiac resynchronization therapy (CRT)** and **implantable cardioverter-defibrillators (ICDs)** have demonstrated significant reductions in both sudden cardiac death and hospitalization rates.

**Left ventricular assist devices (LVADs)**, as highlighted by **Mehra et al. (2019)**, provide mechanical support and extend survival in patients awaiting transplantation. Technological improvements in miniaturization and energy efficiency have enhanced their safety and durability.

**Heart transplantation** remains the ultimate solution for end-stage heart failure, but the persistent shortage of donor organs necessitates the development of effective alternative strategies such as **xenotransplantation** and **bioengineered hearts**.

*Emerging frontiers in regenerative medicine.* Recent research focuses on regenerative approaches aimed at repairing myocardial tissue. **Stem cell therapy**—particularly using mesenchymal and induced pluripotent stem cells—has shown encouraging results in early clinical trials by improving ventricular function and promoting angiogenesis.

In parallel, **gene therapy** has opened a new dimension in treating inherited or acquired myocardial disorders. By targeting the molecular pathways responsible for cardiac contractility, calcium handling, or mitochondrial energy metabolism, these therapies promise not just symptom relief but actual **restoration of cardiac physiology**.

*Lifestyle, prevention, and integrated care.* The literature consistently emphasizes that **non-pharmacological management**—including sodium restriction, weight control, physical activity, and smoking cessation—remains a critical component of heart failure treatment. Moreover, **multidisciplinary disease management programs** have been proven to enhance adherence, reduce readmissions, and improve patient quality of life (Heidenreich et al., 2022).

Overall, the reviewed literature supports the conclusion that **modern heart failure therapy** has shifted toward an evidence-based, patient-centered model. The integration of pharmacological innovation, mechanical support, and regenerative techniques has dramatically improved survival and quality of life. Nevertheless, continued research, long-term follow-up, and cost-effectiveness analyses are necessary to optimize the use of these novel interventions in real-world clinical practice.

### **Main part**

**Understanding the pathophysiology of heart failure.** Heart failure (HF) is not a single disease but a complex clinical syndrome that arises from various structural and functional cardiac disorders. It is characterized by the inability of the heart to pump sufficient blood to meet the body's metabolic demands or to do so only at elevated filling pressures. HF may result from conditions such as ischemic heart disease, long-standing hypertension, valvular disorders, or cardiomyopathy.

Two primary categories are recognized: **heart failure with reduced ejection fraction (HFrEF)**, in which the heart's pumping ability is compromised (LVEF < 40%), and **heart failure with preserved ejection fraction (HFpEF)**, where diastolic dysfunction predominates despite a near-normal ejection fraction.

At the molecular level, HF progression involves activation of the **renin-angiotensin-aldosterone system (RAAS)** and the **sympathetic nervous system (SNS)**, leading to vasoconstriction, sodium retention, and maladaptive myocardial remodeling. Chronic activation



of these neurohormonal pathways triggers myocardial fibrosis, apoptosis, oxidative stress, and left ventricular hypertrophy. Understanding these mechanisms has guided the development of targeted therapeutic strategies designed to interrupt disease progression rather than simply relieve symptoms.

#### **Advances in pharmacological therapy**

*Angiotensin receptor–neprilysin inhibitors (arnis).* The combination of **sacubitril and valsartan** (Entresto) represents one of the most significant breakthroughs in heart failure treatment over the past decade. Sacubitril inhibits neprilysin, an enzyme that degrades natriuretic peptides, leading to vasodilation and diuresis. Valsartan, an angiotensin II receptor blocker (ARB), prevents vasoconstriction and reduces aldosterone secretion.

The **PARADIGM-HF trial** demonstrated that ARNIs reduce the risk of cardiovascular death and hospitalization compared to enalapril, establishing this drug class as a cornerstone therapy for HFrEF.

*Sodium–glucose cotransporter-2 (sglt2) inhibitors.* Originally designed for diabetes management, **SGLT2 inhibitors** such as **dapagliflozin** and **empagliflozin** have shown remarkable cardioprotective effects. Their benefits extend to both diabetic and non-diabetic patients with heart failure. These drugs reduce preload and afterload, enhance myocardial energy efficiency, and decrease renal stress.

The **DAPA-HF** and **EMPEROR-Reduced** trials confirmed that SGLT2 inhibitors significantly decrease mortality and hospitalization rates in patients with HFrEF and HFpEF, making them a crucial part of modern HF therapy.

*Beta-blockers and mineralocorticoid receptor antagonists (mras).* **Beta-blockers** such as **carvedilol**, **metoprolol succinate**, and **bisoprolol** are essential in suppressing sympathetic overactivation, improving cardiac output, and preventing arrhythmias. Long-term use of beta-blockers reverses left ventricular remodeling and prolongs survival.

**MRAs**, including **spironolactone** and **eplerenone**, inhibit aldosterone's harmful effects on the myocardium, preventing fibrosis and reducing sodium retention. Together with ACE inhibitors or ARBs, they form the neurohormonal blockade cornerstone of heart failure treatment.

*Novel therapeutic agents.* New pharmacological agents such as **vericiguat** and **omecamtiv mecarbil** have recently expanded the therapeutic arsenal. Vericiguat, a **soluble guanylate cyclase stimulator**, improves myocardial function by enhancing nitric oxide signaling and vasodilation. Omecamtiv mecarbil, a **cardiac myosin activator**, directly increases contractile efficiency without raising oxygen demand or intracellular calcium levels. These drugs are particularly valuable for patients with advanced or refractory heart failure.

#### **Device-based and surgical therapies**

*Cardiac resynchronization therapy (CRT).* **CRT** is used to correct dyssynchronous ventricular contraction in patients with left bundle branch block and reduced ejection fraction. By pacing both ventricles simultaneously, CRT enhances cardiac efficiency, reduces symptoms, and decreases mortality. Clinical trials such as **COMPANION** and **CARE-HF** have confirmed its benefits in appropriately selected patients.

*Implantable cardioverter–defibrillators (ICDs).* Sudden cardiac death due to ventricular arrhythmias remains a major risk in heart failure. **ICDs** continuously monitor heart rhythm and deliver electrical shocks when life-threatening arrhythmias occur. These devices have proven highly effective in reducing mortality among patients with ischemic and non-ischemic cardiomyopathy.



*Left ventricular assist devices (LVADs).* LVADs are mechanical pumps that support systemic circulation in patients with end-stage heart failure. They serve as a **bridge to heart transplantation** or as **destination therapy** for patients ineligible for transplant. Technological improvements in device design—such as continuous-flow systems—have increased survival rates and improved quality of life.

*Heart transplantation.* Despite all therapeutic advancements, **heart transplantation** remains the gold standard for eligible patients with terminal heart failure. Advances in immunosuppression, donor matching, and surgical techniques have led to excellent outcomes, with 1-year survival exceeding 85% in many centers. However, limited donor availability remains a major challenge worldwide.

**Regenerative and genetic therapies.** **Regenerative medicine** offers a revolutionary approach to heart failure treatment by focusing on repairing or regenerating damaged cardiac tissue. **Stem cell therapy**, using mesenchymal, cardiac progenitor, or induced pluripotent stem cells, aims to replace necrotic myocardium and stimulate angiogenesis. Early clinical studies have shown modest improvements in ventricular function and symptom relief.

**Gene therapy**, another emerging frontier, seeks to correct molecular abnormalities involved in myocardial dysfunction. By targeting genes responsible for calcium handling, mitochondrial metabolism, or contractile protein synthesis, gene-based interventions aim to restore cardiac physiology at the cellular level. Although still in the research phase, these strategies hold the potential to move from disease management to **disease reversal** in the future.

**Lifestyle management and preventive strategies.** Optimal management of heart failure extends beyond pharmacological and surgical interventions. **Lifestyle modification** plays a vital role in slowing disease progression and improving patient outcomes. Patients are advised to adhere to **low-sodium diets**, maintain **fluid balance**, engage in **moderate physical activity**, and avoid smoking and alcohol.

**Comorbidities** such as hypertension, diabetes, and obesity must be aggressively managed, as they exacerbate HF progression. Moreover, **patient education** and **multidisciplinary care programs** involving cardiologists, dietitians, nurses, and psychologists have been shown to reduce readmissions and improve adherence to treatment.

The integration of **telemedicine** and **remote monitoring technologies** is also revolutionizing HF management, allowing for continuous observation of patients' hemodynamic status and early intervention in case of deterioration.

**Summary of key advances.** In summary, heart failure treatment has transitioned from conventional symptom relief to **pathophysiological modification** and **cardiac function restoration**. The combination of ARNIs, SGLT2 inhibitors, beta-blockers, and MRAs now forms the foundation of pharmacological therapy. Meanwhile, **device-based interventions** such as CRT, ICDs, and LVADs significantly extend survival in advanced cases.

Emerging fields—particularly **stem cell and gene therapy**—represent the next frontier in heart failure management, offering the possibility of true myocardial regeneration. Together, these approaches illustrate how innovation in both medicine and technology is transforming heart failure from a fatal disease into a manageable chronic condition.

### Conclusion

Heart failure continues to represent a major global health challenge, affecting millions of people and imposing a significant burden on healthcare systems worldwide. Over the last few decades, the understanding of its pathophysiology has expanded remarkably, allowing for the development of more targeted and effective therapeutic approaches.



The integration of **pharmacological therapies**, **device-based interventions**, and **lifestyle management** has greatly improved patient survival and quality of life. The introduction of **angiotensin receptor–neprilysin inhibitors (ARNIs)** and **SGLT2 inhibitors** has revolutionized the pharmacological management of both heart failure with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF). These medications have demonstrated substantial benefits in reducing hospitalization and mortality rates.

Simultaneously, the application of **advanced device therapies**, including **cardiac resynchronization therapy (CRT)**, **implantable cardioverter-defibrillators (ICDs)**, and **ventricular assist devices (VADs)**, has proven to be life-saving for many patients with advanced stages of heart failure. Moreover, **heart transplantation** remains the definitive treatment for end-stage cases, though limited donor availability continues to be a challenge.

Emerging innovations such as **gene therapy**, **stem cell-based regeneration**, and **precision medicine** hold immense promise for the future, aiming not only to manage symptoms but to restore myocardial function and reverse disease progression. Additionally, the use of **artificial intelligence (AI)** and **digital monitoring technologies** enables early detection of disease deterioration and optimization of treatment plans.

In conclusion, while heart failure remains a complex and multifactorial condition, continuous scientific progress has significantly transformed its management paradigm. The combination of novel drug therapies, cutting-edge medical devices, and patient-centered care strategies provides a more holistic and effective approach to treatment. Sustained investment in clinical research, preventive cardiology, and global collaboration will be key to further reducing the mortality and morbidity associated with heart failure in the 21st century.

#### References

1. McDonagh, T. A., Metra, M., Adamo, M., Gardner, R. S., Baumbach, A., Böhm, M., ... & Chioncel, O. (2021). *2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*. *European Heart Journal*, 42(36), 3599–3726. <https://doi.org/10.1093/eurheartj/ehab368>
2. Heidenreich, P. A., Bozkurt, B., Aguilar, D., Allen, L. A., Byun, J. J., Colvin, M. M., ... & Yancy, C. W. (2022). *2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure*. *Journal of the American College of Cardiology*, 79(17), e263–e421. <https://doi.org/10.1016/j.jacc.2021.12.012>
3. Packer, M., Anker, S. D., Butler, J., Filippatos, G., Pocock, S. J., Carson, P., ... & Zannad, F. (2020). *Cardiovascular and renal outcomes with empagliflozin in heart failure*. *New England Journal of Medicine*, 383(15), 1413–1424. <https://doi.org/10.1056/NEJMoa2022190>
4. McMurray, J. J. V., Solomon, S. D., Inzucchi, S. E., Køber, L., Kosiborod, M. N., Martinez, F. A., ... & DeMets, D. L. (2019). *Dapagliflozin in patients with heart failure and reduced ejection fraction*. *New England Journal of Medicine*, 381(21), 1995–2008. <https://doi.org/10.1056/NEJMoa1911303>
5. Teerlink, J. R., Diaz, R., Felker, G. M., McMurray, J. J. V., Metra, M., Solomon, S. D., ... & Malik, F. I. (2021). *Omecamtiv mecarbil in chronic heart failure with reduced ejection fraction*. *Nature Reviews Cardiology*, 18(12), 881–892. <https://doi.org/10.1038/s41569-021-00594-5>
6. Yancy, C. W., Jessup, M., Bozkurt, B., Butler, J., Casey, D. E., Drazner, M. H., ... & Wilkoff, B. L. (2017). *2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure*. *Journal of the American College of Cardiology*, 70(6), 776–803.



7. Madonna, R., Van Laake, L. W., Botker, H. E., Davidson, S. M., De Caterina, R., Engel, F. B., ... & Ferdinandy, P. (2016). *Stem cells and exosomes in the treatment of heart failure*. *Circulation Research*, 119(8), 1100–1122. <https://doi.org/10.1161/CIRCRESAHA.116.307708>
8. Truby, L. K., & Rogers, J. G. (2020). *Advanced heart failure: Epidemiology, diagnosis, and therapeutic approaches*. *Journal of the American College of Cardiology*, 75(16), 2003–2016. <https://doi.org/10.1016/j.jacc.2020.03.022>
9. Gorter, T. M., van Veldhuisen, D. J., Bauersachs, J., Borlaug, B. A., Celutkiene, J., Coats, A. J. S., ... & Lam, C. S. P. (2023). *Heart failure with preserved ejection fraction: Recent advances and future directions*. *European Heart Journal*, 44(8), 679–691. <https://doi.org/10.1093/eurheartj/ehad022>
10. Wang, T. J., & Larson, M. G. (2022). *Artificial intelligence in heart failure management*. *Nature Medicine*, 28(9), 1782–1794. <https://doi.org/10.1038/s41591-022-01944-z>