ISSN: 2754-6667

Journal of Critical Care & Emergency Medicine

SCIENTIFIC Research and Community

Research Article

Open Access

Congestive Heart Failure and the Goal-Directed Medical Therapy

Osama Alkobari[1], Pankit Wadhwa[2], Husam Shehadeh[3], Aisha Jamal[4], Hira Jamil[5], Muhammad Ammar Husnain[6], Zeinab Salehpour[7] and Marjan Assefi[8]*

[1]Faculty of Medicine,Near East University

[2]MBBS, Muzaffarnagar Medical College, Muzaffarnagar, Affiliated to Chaudhary Charan Singh University, Meerut

[3]MD, Near East University

[4]MBBS, Army Medical College, Affiliated to National University of medical sciences, Rawalpindi, Pakistan

[5]MBBS, University Medical & Dental College Faisalabad, degree allotted by University of Health Sciences Lahore, Pakistan

[6]MBBS, CMH Lahore Medical College, Degree allotted by University of Health Sciences Lahore, Pakistan

[7]Clinical Research Development Unit Beheshti Haspital, Yasuj University of Medical Sciences, Yasuj, Iran

[8]PhD, University of North Carolina at Greensboro, North Carolina

ABSTRACT

Heart failure is one of the top causes of death around worldwide. Heart failure affects approximately 26 million people worldwide today. Considering that obesity, hypertension, diabetes, and smoking all significantly increase the likelihood of heart failure, lifestyle modifications can significantly improve the health of the population. In addition, with an aging population and rising rates of diseases like diabetes and coronary heart disease, it is predicted that the condition's prevalence and costs would increase. As a condition that threatens life, heart failure must consequently be a worldwide health priority. Heart failure is primarily a treatable medical illness. ACE inhibitors and beta-blockers have been found to lower mortality and hospitalization in the treatment of heart failure. The therapy of heart failure seeks to both prolong life by decreasing the progression of the disease and enhance the quality of life of patients by reducing symptoms. Patient education, diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, beta-blockers, aldosterone antagonists, sodium-glucose cotransporter-2 inhibitors, neprilysin inhibitors, sinus node inhibitors, specialized implantable pacemakers/defibrillators and other devices, and correction of the cause(s) of the HF syndrome are all included in the treatment of heart failure.

***Corresponding author**

Marjan Assefi, PhD, University of North Carolina at Greensboro, North Carolina. E-mail: massefi@aggies.ncat.edu

Received: December 29, 2022; **Accepted:** December 30, 2022; **Published:** January 13, 2023

Keywords: Heart Failure, Medical, Therapy, Congestive Heart Failure, Goal Directed Therapy

Introduction

Congestive heart failure, a leading cause of morbidity and mortality, is defined as the inability of the heart muscles to efficiently pump blood out with each contractility. Over 6.5 million people in the United States alone have been affected by Heart failure, resulting in a growing global public health challenge [1]. Congestive heart failure can be caused by underlying coronary artery disease, dilated cardiomyopathy, valvar lesions, and structural abnormalities [2]. The structural and functional changes in the heart lead to the impaired ejection of blood into the body.

The back-flow of blood leads to pressure on the lungs, resulting in dyspnea and cough. The symptoms mainly depend upon the side of the heart affected [3]. According to the Heart Failure Society of America (HFSA), a healthy heart pumps out about 60% of blood from the left ventricle. Broadly, heart failure is divided into two categories: preserved ejection fraction HFpEF (EF >50%) and reduced ejection fraction HFrEF (EF 40% or less) [4]. Prompt diagnosis and early initiation of medical therapy play a pivotal role in alleviating the symptoms and improving the overall quality of life in the majority of patients [5]. Advancements in understanding the pathophysiology and therapies for the disease in the past 30 years have led to Guideline-directed medical treatment GDMT focused on treating the underlying cause and also correcting the failing heart syndrome itself [6]. Current guidelines have recommended the use of four evidence-based drugs: angiotensin II receptor blockers (ARBs) with or without neprilysin inhibitors, beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 inhibitors in patients with reduced ejection fraction (HFrEF) [7].

The main objective of this paper is to summarize the established guideline-directed medical therapies to reduce morbidity and mortality associated with congestive heart failure [8].

The reasons for selection of the study subject were discussed. In addition, the topic's hypothesis, thesis, and research questions were presented and they demonstrated that even though medical professionals have been successful in developing superior management and therapeutic procedures for congestive heart failure (CHF), advanced strategies are still required to reduce the number of readmissions and ensure that elderly patients lead high-quality lives. The primary audience for this research paper will be healthcare professionals who work in various facilities or settings. The concepts and ideas gleaned from the completed research can greatly benefit these practitioners. practitioners from various cultural and socioeconomic backgrounds will be empowered to implement effective strategies to reduce readmissions (Al-Damluji et al.,2015) furthermore, they will provide relevant patient education, locate new technologies, and engage in efficient procedures to produce meaningful outcomes. In addition, these healthcare professionals will use the information presented to improve therapies for managing CHF and conduct ongoing research. The new ideas will eventually help more people with this condition meet their health needs.

Material Methods

The primary and secondary data used in this study were gathered from two distinct sources. Journal articles, books, and trustworthy online sources served as secondary data sources. Because they provided the fundamental information that was required before collecting data from primary sources, they formed the basis of this study. A sample of respondents served as the source for the primary data. Respondents were selected by the researcher from a nearby hospital. The sample consisted of clinical officers, doctors, and nurses who had handled CHF patients previously. CHF patients were also included in the sample. To gather primary data from these respondents, an in-person interview was carried out.

To confirm the hypothesis that was established, the primary data that was gathered from the respondents needed to be analyzed. The primary data findings were subjected to statistical data analysis to see if they supported the hypothesis. For the analysis of the primary data, a regression analysis was used.

The healthcare professionals who work in various facilities that care for CHF patients are the focus of this study [9]. Family practitioners, cardiologists, internists, nephrologists, critical care nurses, and hospital administrators are among these specialists. The objective is to guarantee that they are offered data that will empower them to embrace proof-based practice while offering care to CHF patients. The objective is to minimize hospital readmissions of CHF patients to the greatest extent possible.

Results

In the treatment of congestive heart failure, it is essential to comprehend pharmacotherapy. According to De and Omland (2018), the majority of the currently conducted randomized controlled clinical trials have not sufficiently targeted older CHF patients. However, recent research has attempted to address this issue by demonstrating how it can be addressed specifically for adults.

Diuretics, an angiotensin-angiotensin system inhibitor (ARNI), an angiotensin-converting enzyme (ACE) inhibitor, or angiotensin II receptor blocker (ARB), and a beta-blocker are the primary components of the primary combination therapy for HFrEF. If ACE inhibitor, ARNI, and ARB therapies are contraindicated, the combination of hydralazine and nitrate can be used as primary therapy instead of an angiotensin system blocker.

According to Levine (2016), Diuretics are frequently prescribed for the management of CHF patients. Digoxin or beta-blockers may need to be given at times, according to Katritsis (2016). Spironolactone and angiotensin receptor blocker (ARB) therapy are two other common treatments (Azad & Lemay, 2014).

In African American patients with symptomatic HFrEF who are currently receiving the most effective medical treatment, the combination of nitrate and hydralazine is also recommended for reducing mortality and morbidity. In extreme cases, it may be necessary to perform surgery to remove the obstruction.

When compared to treatment with ACE inhibitors alone, the combination of ARB-ARNI significantly reduced cardiovascular deaths and HF hospitalizations. Patients with LVEFs of less than or equal to 35% and NYHA functional class II to IV are candidates for mineralocorticoid receptor antagonists like spironolactone or eplerenone. After a myocardial infarction (MI), they are also recommended for patients with symptomatic HF and an LVEF of less than 40%. However, these medications were ineffective in patients with a recent MI, a low EF, and no HF symptoms.

A study was published in Sweden in 2022 regarding the use of guideline-directed medical therapy (GDMT) across age groups in patients with reduced ejection fraction heart failure (HFrEF) (Stolfo, Lund et al. 2022). [10]The study demonstrated that out of 27430 people who fit the inclusion criteria of the cohort study, 88% received either renin-angiotensin receptor inhibitor (RASI) or angiotensin receptor neprilysin inhibitor (ARNI), 17% only used ARNI, and 92% used beta-blockers and 45% used mineralocorticoid receptor antagonist (MRA). The use of treatments was lower overall in the older group compared to the young group. Use of renin–angiotensin system/angiotensin receptor–neprilysin inhibitors, beta-blockers, and mineralocorticoid receptor antagonists were 80%, 88%, and 35% in age ≥80 years; 90%, 93%, and 47% in age 70–79 years; and 95%, 95% and 54% in age<70 years, respectively.

A randomized controlled trial (RCT) was conducted in Hannover, Germany in 2017 (Berliner and Bauersachs 2017) which investigated new guidelines of the European Society of Cardiology (ESC) where novel medications are reducing morbidity and mortality in patients with heart failure [11]. The angiotensin-receptor neprilysin inhibitor (ARNI) is being compared to Angiotensin-converting enzyme inhibitors (ACEi) to determine the impact on global mortality and morbidity in heart failure (PARADIGM-HF) and in a phase 3 RCT to understand the efficacy of the ARNI. Participants of 8442 were selected according to the inclusion criteria of having symptomatic HF (NYHA class IIII–IV a reduced left ventricular function (LVEF ≤40%, changed to ≤35% during the study), brain natriuretic peptide (BNP) ≥150 pg/mL or N-terminal proBNP (NT-proBNP) ≥600 pg/mL (≥100 respectively 400 pg/mL with HF hospitalization in the previous 12 months), and an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m2). The ARNI used was a combination of sacubitril/valsartan and the ACEi used as enalapril. Results showed a significant reduction in the cardiovascular mortality rate by 20% in the patients receiving ARNI, also a reduction in heart failure hospitalizations by 21% in patients who received ARNI and finally a reduction in all-cause

mortality by 16% in patients receiving ARNI in comparison to the patients taking ACEi. As a conclusion to this study, they added the sacubitril/valsartan combination in their new guidelines in patients who meet the inclusion criteria and yet remain symptomatic despite therapy with ACE, ARB, or a beta-blocker, and an MRA.

A systematic review with meta-analysis regarding pharmacological treatment of patients with heart failure with reduced ejection fraction was done to analyze randomized controlled trials published between January 1987 and January 2020 [12]. In the review, the medications included were angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), beta-blockers (BB), mineralocorticoid receptor antagonists (MRAs), digoxin, hydralazine-isosorbide dinitrate, ivabradine, angiotensin receptor–neprilysin inhibitors (ARNi), sodium-glucose cotransporter-2 inhibitors (SGLT2i), vericiguat, and omecamtiv-mecarbil. The main outcome of the review was all-cause death in 75 trials with 95444 participants. Results demonstrated that the combination of ARNi, BB, MRA, and SGLT2i was most effective in reducing all-cause death with a hazard ratio (HR) of 0.39 followed by a combination of ARNi, BB, MRA, and vericiguat with an HR of 0.41, and lowest effectiveness in a combination of ARNi, BB, and MRA with a HR of 0.44. In addition, the outcome of cardiovascular death or first hospitalization in patients with heart failure was the least in patients who used the drug combination of ARNi, BB, MRA, and SGLT2i with a HR of 0.36, followed by a HR of 0.44 for the drug combination of ARNi, BB, MRA, and omecamtiv-mecarbil, and in patients using drug combination of ARNi, BB, MRA, and vericiguat with a HR of 0.43. As a result, in patients with heart failure with reduced ejection fraction, the greatest efficacy was found with the drug combination of ARNi, BB, MRA, and SGLT2i.

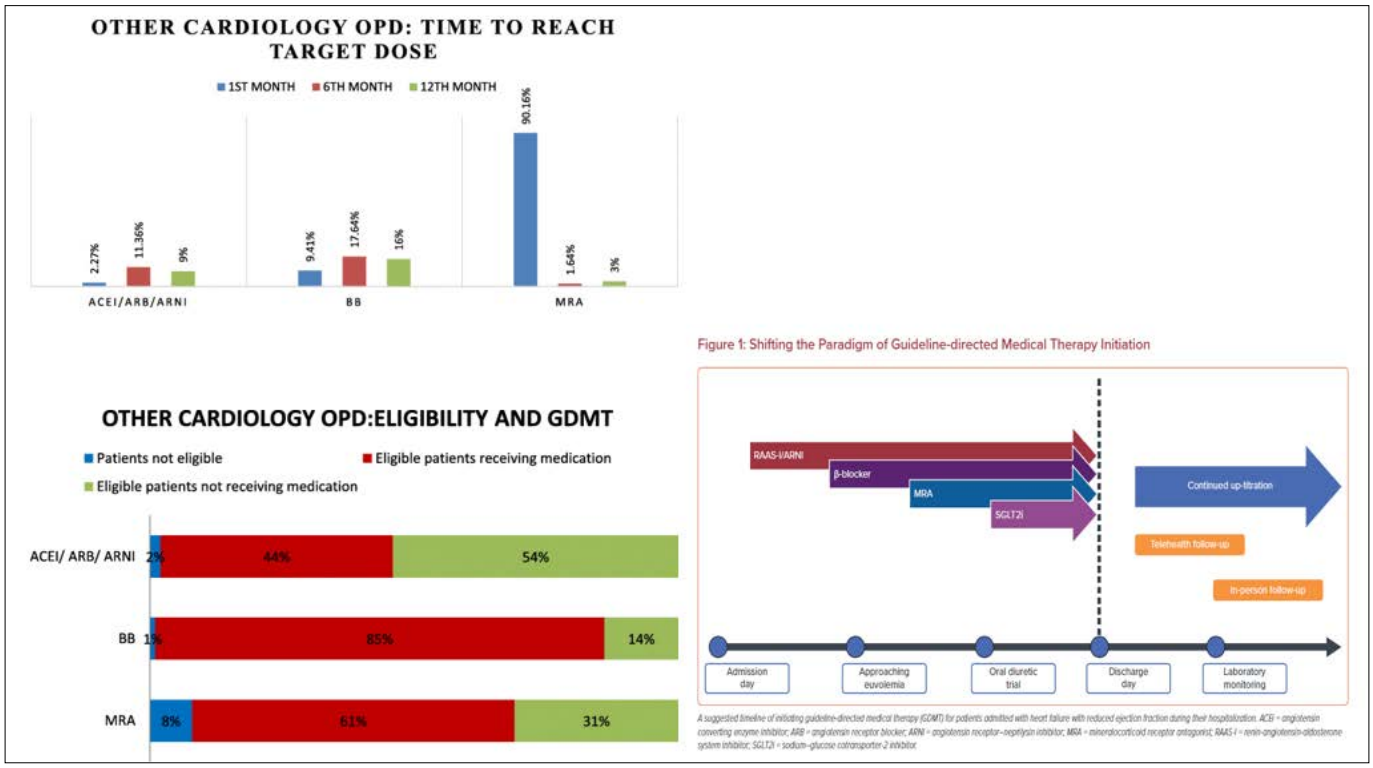

Figure 1: Shifting the Paradigm of Guideline-directed Medical Therapy Initiation

A suggested timeline of initiating guideline-directed medical therapy (GDMT) for patients admitted with heart failure with reduced ejection fraction during their hospitalization. ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor–neprilysin inhibitor; MRA = mineralocorticoid receptor antagonist; RAAS-I = renin-angiotensin-aldosterone system inhibitor; SGLT2i = sodium–glucose cotransporter-2 inhibitor.

Discussion

Due to the rising number of people that are admitted to hospitals for a variety of reasons, the governments are spending a significant amount of money on healthcare [13]. One of the diseases that are becoming more and more common in the countries is congestive heart failure. It is more prevalent in the elderly, particularly those who exercise significantly less. The most pressing issue is the rising number of hospital readmissions. It is expected that once the right medications are given, the person will live a healthy life. However, that may not always be the case. The greater the number of times these patients are readmitted, the greater is the strain on healthcare facilities. To eliminate readmissions, it is essential to enhance the quality of care provided to CHF patients. Patients must also be empowered to lead healthy lifestyles that will prevent CHF from developing. Medical professionals have attributed this health issue mainly to a lack of physical activity and poor eating habits. The accumulation of cholesterol in the body is one of the most common outcomes of limited physical activity, according to De and Omland (2018). As the cholesterol continues to build up, it may cause the blood vessels to become narrow or completely blocked. According to Covell (2016), engaging in physical activity causes the body to produce sufficient heat to prevent the accumulation of body fat in the vessels. During these kinds of physical activities, extra fat can be utilized to produce energy. Muscle weakness is another common side effect of low physical activity. Lamarck's Use and Disuse Theory states that when body organs are not used often, they tend to become inactive. The heart muscle also experiences the same effect. When the body is put through regular exercise, the heart muscle is forced to pump more blood to various body cells, and hence the heart muscles get stronger as a result.

Therefore, both the heart muscle and other muscles in the body are strengthened by regular exercise. When one does not engage in physical activity, the opposite proves true. Heart muscle weakness is common in today's society, where people prefer to spend most of their time on smartphones or in front of televisions leading a sedentary lifestyle. An unhealthy diet, which is loaded with calories and other nutrients that are not good for the body, make the situation even worse [14]. This clarifies why congestive heart

failure is becoming increasingly common, particularly among retired Americans who value their leisure time. The discovery from the essential information examination is that proof-based treatments are basic in upgrading quality consideration while taking care of CHF patients. This makes it simple for various medical professionals to collaborate to provide quality care. In addition, it requires hospital management to be actively involved in ensuring that hospitals have the necessary staff and equipment to provide superior services. CHF patients may experience fewer hospital readmissions because of these strategies.

The reduction of hospitalization, cardiovascular death from a direct cause, and overall mortality are the three basic objectives of congestive heart failure management.

Pharmacologic therapy aims to administer all indicated agents rather than a single agent because the combined effect of these treatments is superior to that of a single agent. As the science and literature on the treatment guidelines of congestive heart failure develop year by year, articles are being published about trends, efficacy, and changes in medications regarding congestive heart failure. One of the most pressing concerns that researchers and practitioners in the medical field have is the lack of established guidelines and procedures for dealing with the issue. Each physician is free to choose the method that best suits his or her practice (Thiriet, 2015).

The study carried out in Sweden in 2022 revealed that the beta-blockers are the most commonly used drug in achieving these goals, followed by an inhibitor of the Renin-Angiotensin System or inhibitor of Angiotensin Receptor-Neprilysin Inhibitors, Angiotensin Receptor-Neprilysin Inhibitors only make up about a fifth of the chunk, followed by Mineralocorticoid Receptor Antagonists [10]. This shows that Beta-blockers take into account almost every different mechanism of injury to the heart and therefore are beneficial in almost all causes and severities of Congestive Heart Failure. In addition, the use of Beta-blockers and Renin-Angiotensin System Inhibitors was equal in patients younger than 70 years whereas older patients used beta-blockers more frequently than renin-angiotensin system inhibitors. This suggests that Beta-Blockers and Renin-Angiotensin System Inhibitors have equal efficacy in achieving these goals in earlier stages of congestive heart failure and causes of Congestive Heart Failure in young patients. Another point to consider is that as the patient ages the overall use of all different medications was less, this may be partly because of intolerance to the adverse effects of these medications or the lesser role of medical interventions in addressing the pathogenesis of advanced stages of Congestive Heart Failure when compared to non-medical interventions. However, this study is subject to residual confusion, as it did not collect the specific reasons for either not prescribing or titrating the therapies. The analyses were also widely modified for many probable reasons for underuse/under-dosing/low tolerability including clinical (blood pressure and heart rate) as well as socio-demographic features and type of follow-up, which may be a substitute for the missing data. Additionally, this study did not take into account heart failure with preserved ejection fraction, its treatment objectives, or how those objectives are to be attained. Selection Bias is also a limitation since the inclusion criteria of the study takes into account only age group and not the other co-morbid conditions and the adverse effects of these medical therapies in these co-morbid conditions that leads to an increase in the overall cause of mortality in Congestive Heart Failure. This leads to the question of the efficacy of the drugs used to achieve the goals of treatment of Congestive Heart Failure with simultaneous co-morbid conditions. To answer this question, multiple comparisons taking into account the Heart Failure with preserved Ejection Fraction and the specific drugs that are to be used for achieving specific goals with the ongoing other conditions should also be performed.

Newer Drugs such as the combination of sacubitril and valsartan which belong to the Angiotensin Receptor-Neprilysin Inhibitor class have been shown to decrease all-cause mortality, hospitalization, and direct cardiovascular death in certain scenarios and therefore also have added in the new treatment guidelines for Congestive Heart Failure after a Randomized Control Trial was perfumed in Germany in 2017 [10]. In the trial mentioned above, no discussion regarding classification-based therapy is mentioned and therefore the overall beneficial effect of this combination is still under questioning since the trial carried out in Germany only included patients that met certain class criteria.

Several randomized trials carried out between January'87 and January'20 revealed that the Angiotensin Receptor Blockers, Beta-Blockers, and Mineralocorticoid Receptor Antagonists when used in combination with Sodium-Glucose Transporter 2 Inhibitors were very effective in reducing all-cause mortality, hospitalization, and direct cardiovascular deaths indicating that the Sodium-Glucose Transporters 2 Inhibitors may have an indirect beneficial effect in reducing the other causes of mortality that might not be directly linked to the disease process associated with direct myocardial damage, again implying that there is more to the pathogenesis of congestive heart failure than just the previously thought Neuro-hormonal insults [11]. To thoroughly understand the therapeutic potential of advanced therapies for the treatment of CHF, well-designed, large-scale, randomized control trials with objective outcomes and considering other risk factors and disease processes should be performed.

Conclusion

Heart failure is a clinical syndrome with a lot of complications and high mortality rates. To achieve the best possible clinical outcomes, a treatment strategy that incorporates patient education, pharmacologic management, and surgical interventions is required. Specialty-prepared HF attendants are fundamental to the inter professional group focusing on patients with HF. They instruct the patient on the significance of way-of-life alterations and clinical consistency to assist with further developing dreariness and mortality for the patient. They also teach the patient how to manage their symptoms and weight to avoid HF exacerbations and hospitalizations. To assist the patient in adhering to the lifestyle changes that have been suggested by the medical team, the HF-trained social worker and case manager can assist with the patient's evaluation during in-home visits and community settings. By reviewing patient medication lists and reducing the likelihood of adverse drug-drug interactions, clinical pharmacists assist medical professionals [14].

In conclusion, beta-blockers, renin–angiotensin receptor inhibitors (RASI) or angiotensin receptor–neprilysin inhibitors (ANRI), mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors (SGLT2i) are the drugs that are widely used for the treatment of congestive heart failure, with Beta-blockers being favored in the older population [15]. These four drugs were most effective in decreasing the overall burden due to cardiovascular deaths and hospitalization [16]. There is a drastic reduction in the morbidity and mortality in patients with CHF, when ARNI is used with Sacubitril/ valsartan and when ACEi is used with enalapril. ARNI is better than ACEi in reducing

cardiovascular mortality and hospitalizations [10]. To provide symptomatic relief, additional agents like, digoxin, hydralazine-isosorbide dinitrate, ivabradine, vericiguat, and omecamtiv-mecarbil, can be added depending on the patient presenting complaints [11]. Efforts are required to make the patients with HFrEF adhere to the optimal therapy to have the most benefits. In large clinical trials, SGLT2i has emerged as the drug with the most effectiveness, making them one of Class 1 recommended drugs by ESC guidelines for patients with chronic HFrEF [17].

Despite pharmacological guidelines, significant gaps in guideline-directed medical therapies and dose prescribed remain. Further healthcare-directed research is needed to improve clinical factors associated with baseline use and dose of GDMT [18]. To optimize the therapeutic potential of medical therapies with the advent of novel drugs further randomized controlled trials need to be conducted with objective outcomes [19]. However, these four drugs, beta-blockers, renin-angiotensin receptor inhibitors (RASI) or angiotensin receptor–neprilysin inhibitors (ANRI), mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors (SGLT2i) remain an essential pillar to decrease morbidity and mortality in patients with CHF [20-53].

References

1. Ami Shah, Dimple Gandhi, Sneha Srivastava, Kunal J Shah, Rupal Mansukhani (2017) Heart failure: a class review of pharmacotherapy. Pharmacy and Therapeutics 42: 464.
2. Ahmad Malik, Daniel Brito, Sarosh Vaqar, Lovely Chhabra, Chaddie Doerr (2022) Congestive heart failure (nursing). Stat Pearls publishing. https://www.ncbi.nlm.nih.gov/books/NBK574497/.
3. King KC, Goldstein S (2021) Congestive heart failure and pulmonary edema. Stat Pearls [Internet]. StatPearls publishing. https://pubmed.ncbi.nlm.nih.gov/32119444/.
4. Andronic AA, Mihaila S, Cinteza M (2016) Heart failure with mid-range ejection fraction–a new category of heart failure or still a gray zone. Maedica (Bucur) 11: 320-324.
5. Brownell NK, Ziaeian B, Fonarow GC (2021) The gap to fill: rationale for rapid initiation and optimal titration of comprehensive disease-modifying medical therapy for heart failure with reduced ejection fraction. Cardiac Failure Review 7: e18.
6. Shannon MDunlay, Jill M Killian, Veronique LRoger, Phillip J Schulte, Saul B Blecker, et al. (2022) Guideline-Directed Medical Therapy in Newly Diagnosed Heart Failure With Reduced Ejection Fraction in the Community. Journal of Cardiac Failure 28: 1500-1508.
7. Eldad Rahamim, Dean Nachman, Oren Yagel, Merav Yarkoni, Gabby Elbaz-Greener et al. (2021) Contemporary pillars of heart failure with reduced ejection fraction medical therapy. Journal of Clinical Medicine 10: 4409.
8. Peter A McCullough, Hirsch S Mehta, Colin M Barker, Joanna Van Houten, Sarah Mollenkopf, et al. (2021) Mortality and guideline□directed medical therapy in real□world heart failure patients with reduced ejection fraction. Clinical Cardiology 44: 1192-1198.
9. Ward C, Witham M (2009) A practical guide to heart failure in older people. John Wiley & Sons https://www.wiley.com/en-us/+Practical+Guide+to+Heart+Failure+in+Older+People-p-9780470695173.
10. Davide Stolfo, Lars H Lund, Peter Moritz Becher, Nicola Orsini, Tonje Thorvaldsenet, al. (2022) Use of evidence□based therapy in heart failure with reduced ejection fraction across age strata. European Journal of Heart Failure 24: 1047-1062.
11. Berliner D, Bauersachs J (2017) Current drug therapy in chronic heart failure: the new guidelines of the European Society of Cardiology (ESC). Korean circulation journal 47: 543-554.
12. Jasper Tromp, Wouter Ouwerkerk, Dirk J van Veldhuisen, Hans L Hillege, A Mark Richards, et al. (2022) A systematic review and network meta-analysis of pharmacological treatment of heart failure with reduced ejection fraction. Heart Failure 10: 73-84.
13. Bhatt DL (2015) Interventional and device therapy in heart failure, an issue of heart failure clinics. Elsevier Health Sciences https://www.elsevier.com/books/interventional-and-device-therapy-in-heart-failure-an-issue-of-heart-failure-clinics/bhatt/978-0-323-35975-7.
14. Andreadis EA (2016) Hypertension and cardiovascular disease. Springer https://link.springer.com/book/10.1007/978-3-319-39599-9.
15. Ki Hong Choi, Jin Oh Choi, Eun Seok Jeon, Ga Yeon Lee, Dong Ju Choi, et al. (2018) Guideline□directed medical therapy for patients with heart failure with midrange ejection fraction: a patient□pooled analysis from the Kor HF and Kor AHF registries. Journal of the American Heart Association 7: e009806.
16. Jeeva Joseph, Stephy PS, Jude James, Suja Abraham, Jabir Abdullakutty (2020) Guideline-directed medical therapy in heart failure patients: impact of focused care provided by a heart failure clinic in comparison to general cardiology out-patient department. The Egyptian Heart Journal 72: 1-8.
17. Danning Yang, Yu Zhang, Jie Yan, Ming Liu, Fengshuang An (2022) SGLT-2 inhibitors on prognosis and health-related quality of life in patients with heart failure and preserved ejection fraction: A systematic review and meta-analysis. Frontiers in Cardiovascular Medicine 9: 942125.
18. Abhinav Sharma, Subodh Verma, Deepak L Bhatt, Kim A Connelly, Elizabeth Swiggum, et al. (2022) Optimizing foundational therapies in patients with HFrEF: how do we translate these findings into clinical care?. Basic to Translational Science 7: 504-517.
19. Dixit, Neal M, Shah, Shivani, Ziaeian (2021) Optimizing guideline-directed medical therapies for heart failure with reduced ejection fraction during hospitalization. US Cardiology Review 15: e07.
20. Paul A Heidenreich, Biykem Bozkurt, David Aguilar, Larry A Allen, Joni J Byun, et al. (2022) 2022 AHA/ACC/HFSA guideline for the management of heart failure: Executive summary: a report of the American College of Cardiology/American heart association joint Committee on clinical practice guidelines. Journal of the American College of Cardiology 79: 1757-1780.
21. Amery A, Fagard R, Lijnen P, Staessen J (2011) Hypertensive cardiovascular disease: Pathophysiology and treatment: Pathophysiology and treatment. Springer https://link.springer.com/book/10.1007/978-94-009-7476-0.
22. Aronow WS, Ahmed A (2017) Heart failure in older adults, an issue of heart failure clinics, E-book. Elsevier Health Sciences https://www.elsevier.com/books/heart-failure-in-older-adults-an-issue-of-heart-failure-clinics/978-0-323-53134-4.
23. Bakris GL, Baliga RR (2019) Hypertensive heart disease is an issue of heart failure clinics. Elsevier Health Sciences https://www.elsevier.com/books/hypertensive-heart-disease-an-issue-of-heart-failure-clinics/978-0-323-68123-0.
24. Baliga RR, Samal UC (2018) Recent advances in the management of heart failure, an issue of heart failure clinics

E-book. Elsevier Health Sciences https://www.elsevierhealth.com.au/recent-advances-in-management-of-heart-failure-an-issue-of-heart-failure-clinics-9780323641258.html.

25. Bussmann W (2011) Acute and chronic heart failure: Diagnosis and therapy. Springer https://link.springer.com/book/10.1007/978-3-642-61627-3.
26. Choi S, Kassan M, Morán AM (2021) Diabetes, hypertension, and cardiovascular diseases. Frontiers Media SA https://www.frontiersin.org/articles/10.3389/fphys.2021.765767/full.
27. Chopra H, Nanda NC, Narula J (2020) Advances & innovations in heart failure (AIHF): A textbook of cardiology. Jaypee Brothers Medical Publishers https://www.jaypeebrothers.com/pgDetails.aspx?book_id=9789389587890.
28. Clark AL, Gardner RS, McDonagh TA (2022) Oxford textbook of heart failure. Oxford University Press https://global.oup.com/academic/product/oxford-textbook-of-heart-failure-9780198766223?cc=us&lang=en&.
29. Congestive heart failure (2002) author index. Congestive Heart Failure 8: 350-351. https://doi.org/10.1111/j.1527-5299.2002.02002.x
30. Dorobanţu M, Ruschitzka F, Metra M (2016) Current approach to heart failure. Springer https://link.springer.com/book/10.1007/978-3-319-45237-1.
31. Drenjančević I (2018) Hyperbaric oxygen treatment in research and clinical practice: Mechanisms of action in focus. BoD – Books on Demand https://directory.doabooks.org/handle/20.500.12854/49735.
32. Felker GM, Mann DL (2019) Heart failure: A companion to Braunwald's heart disease E-book. Elsevier Health Sciences https://www.mea.elsevierhealth.com/heart-failure-a-companion-to-braunwalds-heart-disease-9780323609876.html.
33. heart failure: Symptoms, causes and treatment. Nova Biomedical Books.
34. Garry DJ, Wilson RF, Vlodaver Z (2017) Congestive heart failure and cardiac transplantation: Clinical, pathology, imaging and molecular profiles. Springer https://link.springer.com/book/10.1007/978-3-319-44577-9.
35. Hosenpud JD, Greenberg BH (2000) Congestive heart failure: Pathophysiology, diagnosis, and comprehensive approach to management https://www.semanticscholar.org/paper/Congestive-Heart-Failure%3A-Pathophysiology%2C-and-to-Hosenpud-Greenberg/236b257060170bbfe14d3974dffc3d10d5c9b89f#citing-papers.
36. Hosenpud JD, Greenberg BH (2007) Congestive heart failure. Lippincott Williams & Wilkins.
37. Kaski JC (2010) Coronary artery disease: Chronic stable angina. Drugs in Cardiology 31-44 https://doi.org/10.1093/med/9780199557462.003.0026.
38. Khan MG (2007) Heart disease diagnosis and therapy: A practical approach. Springer Science & Business Media. https://link.springer.com/book/10.1385/1592598684
39. Lecker SH, Chang BJ (2021) The ultimate medical school rotation guide. Springer Nature. https://link.springer.com/book/10.1007/978-3-030-63560-2.
40. Lopez AD (2006) Global burden of disease and risk factors. World Bank Publications.
41. Maisel AS, Filippatos GS (2016) Algorithms in heart failure. JP Medical.
42. Marx N, Reith S (2018) Managing chronic coronary artery disease in patients with diabetes. Chronic Coronary Artery Disease 355-373. https://doi.org/10.1016/b978-0-323-42880-4.00024-8.
43. Ohlstein E, Rossi F (2022) Novel perspectives for the therapy and prevention of heart failure. Frontiers Media SA https://www.frontiersin.org/research-topics/16159/novel-perspectives-for-the-therapy-and-prevention-of-heart-failure.
44. Ram CV, Teo BW, Wander GS (2022) Hypertension and cardiovascular disease in Asia. Springer Nature. https://link.springer.com/book/10.1007/978-3-030-95734-6#:~:text=Asia%20has%20the%20largest%20population,for%20HTN%20and%20CVD%20outbreaks.
45. Gunduz E, Akay OM, Birdane A, Gulbas Z (2011) Stem cell therapy for congestive heart failure. Journal of Stem Cells and Regenerative Medicine 7: 87-89.
46. Stewart S, Sliwa K, Mocumbi A, Damasceno A, Ntsekhe M (2016) The heart of Africa: Clinical profile of an evolving burden of heart disease in Africa. John Wiley & Sons. https://www.wiley.com/en-us/+Heart+of+Africa%3A+Clinical+Profile+of+an+Evolving+Burden+of+Heart+Disease+in+Africa-p-9781119097006.
47. Stott DJ, Lowe GD (2012) Cardiovascular disease and health in the older patient: Expanded from 'Pathy's principles and practice of geriatric medicine' (5th ed.). John Wiley & Sons https://www.wiley.com/en-us/Cardiovascular+Disease+and+Health+in+the+Older+Patient%3A+Expanded+from+%27Pathy%27s+Principles+and+Practice+of+Geriatric+Medicine%2C+Fifth+Edition%27-p-9781118447673.
48. Teerlink JR, Metra M, Filippatos GS, Davison BA, Bartunek, J, et al. (2017) Benefit of cardiopoietic mesenchymal stem cell therapy on left ventricular remodelling: Results from the congestive heart failure Cardiopoietic regenerative therapy (CHART-1) study. European Journal of Heart Failure 19: 1520-1529.
49. Theisler C (2022) Heart failure/Congestive heart failure. Adjuvant Medical Care, 156-160 https://doi.org/10.1201/b22898-170.
50. Ventura HO (2016) Pharmacologic trends of heart failure. Springer https://link.springer.com/book/10.1007/978-3-319-30593-6.
51. Watson KE, Guo Y, Sahni S (2018) Secondary prevention of coronary artery disease. Chronic Coronary Artery Disease 479-487. https://doi.org/10.1016/b978-0-323-42880-4.00030-3.
52. Wilson PW, O Donnell CJ (2018) Epidemiology of chronic coronary artery disease. Chronic Coronary Artery Disease 1-15 https://doi.org/10.1016/b978-0-323-42880-4.00001-7.
53. Shannon MDunlay, Jill M Killian, Veronique LRoger, Phillip J Schulte, Saul B Blecker, et al. (2022) Guideline-Directed Medical Therapy in Newly Diagnosed Heart Failure With Reduced Ejection Fraction in the Community. Journal of Cardiac Failure 28: 1500-1508.